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The Arthur E. Mills Memorial Oration.[1]

A SCIENTIST LOOKS AT NATURE.

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AT the end of the last century the march of science had intoxicated mankind. In the physical sciences, the great success of the application of mathematical reasoning to experimental observations, particularly in thermodynamics, celestial mechanics, the kinetic theory of gases and the electromagnetic theory of light, had bred a certainty that the ultimate knowledge of nature was very close, if not actually at hand. The French mathematician, Laplace, believed that if the position and motion of every atom in the universe were known, at a given instant, it would be possible to predict the whole future of the cosmos. Every event was preceded by a cause and each event led inevitably to a particular other event. The whole course of the history of matter was thus predetermined and inevitable. Materialism and dialectical argument were the result.

In the biological sciences, the work of Darwin had made the living entities of today the unavoidable consequences of the appearance of the first unicellular organism on this earth, while the emergence of modern medicine and surgery had bred a belief in man's complete mastery over his destiny. It seemed inevitable that the advancing technologies of Europe would ensure for ever the dominance of the clever West over the less inspired nations of the world.

This conception of an arrogant and amoral science, rapidly enmeshing mankind in a web of materialism to satisfy its enormous ego, still persists among very many today. I am continually told by correspondents that men of science are those whose ideas are so inflated that they vie with God in determining the future of mankind, and I am told by colleagues that they receive similar ranting letters of abuse. Often, those who write claim that through the scriptures, the dogmas of their church, clairvoyance, communion with spirits or revelation, they are in possession of knowledge far more fundamental and far-reaching than any of the "laws" of science. It is strange that even among educated men, deeply versed in literature and scholarship, there is distrust of science for the cruel inevitability of its

[1] Delivered on May 27, 1959, at the Annual Ceremony of The Royal Australasian College of Physicians, in the Bonython Hall, University of Adelaide.

predictions, which they believe sincerely to be undermining the whole basis of civilization and of graciousness in existence. This, despite the enormous volume of books, radio talks, newspaper articles and lectures, by which they are supposed to be informed about the methods and objectives of science and the nature of the man of science.

This state of affairs is as much the fault of the scientist as of the ordinary man. He has allowed technology, the practical fruit of scientific knowledge, to become the non-scientist's picture of science itself. Rockets and space-travel obscure vision of the transcendental beauty of our knowledge of the physical universe, while the masked and white-robed surgeon, and the vivisectionist, are the layman's picture of the biological scientist. The terrible reality of the threat of nuclear weapons makes the nuclear scientist an object of suspicion and even hatred. Many who venerate the physician at the bedside, harbour the blackest conceptions of medical research or of experimenting with living men.

Sir C. P. Snow, scientist, administrator and novelist, has said that today the people of the western nations are no longer divided into the rich and the poor, but into those who are ignorant of science and those who understand something about science and the way it works. He regards this as the great rift in modern civilization which must somehow be closed.

I do not know how it will be possible to give to all men some understanding of science, except by a great expansion of teaching about science, rather than of science, in our schools and universities. However, it does seem worthwhile to say something to this learned gathering about the nature of modern science and the way it looks at the world.

Today the astronomer observes with the largest telescopes objects which are so far away that light, travelling at 180,000 miles every second, has taken nearly one thousand million years to arrive at the earth. At those immense distances, there is no sign of any falling off in the number of galaxies of stars which populate space. In other words, there is no evidence that the universe is finite. "World without end." The particle physicist is concerned with objects so small that one million million of them placed side by side would measure less than an inch, and there is no evidence that he has yet penetrated to the most minute, or to the ultimate matter of which all else is made. Using the methods of modern science, man can now contemplate objects in space over a range in size of 3×10^{37}—that is, 3 million ... (million repeated 37 times) ... times. Such immensity is awe-inspiring, and makes every man of sensibility feel deep humility. At the same time, such contemplation sets man apart, for he alone can imagine dimensions outside himself.

As knowledge of the very small and the very large has increased, it has been found necessary to modify progressively almost all the most cherished "laws" of classical physics. The laws governing the behaviour of ordinary matter cannot be applied to the cosmos or to the atom, although they continue to describe accurately the trajectory of an artificial satellite or the movements of the parts of machines. Causality has been redefined and determinism has given way to uncertainty.

The realization that an attempt to describe the behaviour of an assemblage of atoms, such as a gas in a closed vessel, by adding up the motions and interactions of all individual atoms, is impossible in practice, led to the development of statistical laws which applied to the system as a whole. Thus, while each individual action between atoms was assumed to obey Newton's laws, it was easier, for instance, to describe statistically, as the pressure, the total of the thrusts of individual atoms against the walls of the vessel. Similarly, the average energy of motion of the atoms can be defined statistically as the temperature. The process is similar to that by which we describe the average annual rainfall of Adelaide as 22 inches of water, without reference at all to the days when it rained or the number of drops of rain which fell on June 16, 1907, in a given direction on a certain area. The statistical picture enables scientists to reason about all sorts of systems, of atoms or insects or human beings, for instance, though our knowledge of individual behaviour is far from complete. However, while we could, in theory, describe the behaviour of every human being, we now know that statistical behaviour is built, as it were, into atoms and their constituents, so that it is impossible ever to predict the individual behaviour of atomic particles.

The multitude of atoms on the surface of a heated filament of an electric lamp radiates energy as light. The quantum ideas, originated by Max Planck early in this century, tell us that the apparently continuous stream of radiation consists, in fact, of tiny bundles of energy which move through space as individual units, or quanta. The light we observe is the statistical result of millions of such quanta. These quanta are emitted by each atom, but it is impossible to predict just when any given atom will emit a quantum of radiation. While the total emission of light can be accounted for quantitatively as the consequence of the heat motions of the constituent atoms and electrons of the surface of the filament, when we attempt to describe the emission from a given atom we are faced with uncertainty.

The process of observing an atom implies interference with its position or its motion, or both. An attempt to observe accurately its position is found to leave its state of motion uncertain, while to measure its velocity with precision its position must be indeterminate. According to the quantum theory, in any observation the product of the uncertainty in position, multiplied by the uncertainty in velocity, cannot be less than the quantity called Planck's constant. It is found in practice that conclusions derived from this "uncertainty principle" are verified, and there is abundant evidence of the validity of this strange concept. It follows at once that the behaviour of elementary particles cannot be described by application of Newton's laws of motion, which require that position and velocity be known at every instant.

All sorts of attempts have been made to reconcile the mechanics of atoms and their constituents with the ideas of classical physics, but physicists are now persuaded that there is no way out except through the established concepts of quantum theory. It is possible only to speak of the probability of a particle being in a certain position or having a defined velocity. The scientist now accepts the new rules of conduct laid down by the quantum theory for particles, because he finds that they give him the correct answers in almost all cases. The smeared-out character of the world of particles has been best expressed by the development of the quantum wave-mechanics, according to which the behaviour of elementary particles can be calculated if they possess many of the characteristics of wave motion, while the behaviour of electromagnetic waves can often be best described by assuming that they consist of discrete, particle-like quanta. For instance, it is impossible to predict at what instant a given atom of radium will disintegrate, but a very satisfying reason for this is given by application of wave-mechanical ideas, and it becomes practicable to calculate the probability that the atom will disintegrate in a given time. It can be stated with certainty that half the atoms in a gramme of radium will disintegrate in 2000 years, but it is not possible to say which particular atoms will disintegrate. On the other hand, when light falls upon a suitable conducting surface, as in a photoelectric cell, electrons are released from the surface with a definite maximum energy, depending only on the wavelength of the radiation and not on its intensity. This photoemission of electrons can be explained only by the assumption that the radiation consists of particle-like quanta of energy, each of which reacts with a single electron. No explanation is possible with the picture of light as an electromagnetic wave-motion, although this explains most successfully many other properties of light.

This strange duality of nature is not easy to grasp. Students and physicists develop a kind of schizophrenia in order to deal with it. However, our friends the chemists and biologists now take over these new concepts of physics to explain successfully such phenomena as chemical binding forces, the behaviour of ions at the membrane surfaces of living cells, or the detection of light by the eye. The underlying philosophical problems involved tend to be lost sight of the further the ideas move away from the realm of pure physics.

Two cherished laws of physics, upon which the whole of engineering, chemistry and much of biology have been built, are the laws of conservation of matter and of energy. These laws are verified exactly in ordinary experience, but there is reason now to doubt their universal validity. The interconvertibility of mass and energy, postulated by the theory of relativity, was demonstrated in the mass changes associated with nuclear reactions, and in the discovery that the electromagnetic energy of X-rays of short wavelength could be transformed into pairs of electrons, electrically charged one positively and the other negatively. Since then, it has been found that a number of particles called mesons, which live for very short intervals of time only, can be made artificially from energy in pairs as particles and antiparticles. Even the proton itself (the fundamental unit of positive charge and the simplest of nuclear particles, being the nucleus of the hydrogen atom) can now be created, together with its antiparticle, the negative proton, out of energy alone. This strange symmetry in nature, whereby each of the fundamental particles of which matter is composed can exist as both the "natural" particle and its antiparticle, was predicted theoretically by Dirac before the discovery of antiparticles, on the basis of a form of quantum mechanics which takes account of the concepts of relativity.

A particle and its antiparticle, when they collide with one another, can combine together, mutually annihilating each other and producing an equivalent amount of energy as two quanta of hard X rays. Thus matter can be created out of energy and can be converted into energy.

The laws of conservation of matter and of energy must now be regarded as parts of a more general conservation of mass-energy. However, even this wider interperation of conservation may be invalid under some circumstances, as will be seen later.

The aim of science is to give an "explanation" of the physical world with the fewest possible concepts. The 98 different species of chemical elements can be built up from three elementary particles — the proton, carrying a positive charge, the neutron, of approximately the same mass as the proton but with no electric charge, and the negatively-charged electron with a mass about 1/1840 of that of the proton. It is possible that these three fundamental particles, from which all matter as we know it is built, may themselves be different energy states of one elementary substance. Most concepts of the origin of the universe have been based on the assumption that a great mass of hydrogen gas assembled in space, was heated by gravitational contraction, and, at the very high temperatures of hundreds of millions of degrees centigrade generated at the core, thermonuclear "fusion" processes produced heavier chemical elements by combination of the hydrogen atoms, with the release of enormous quantities of energy. The assembled matter was then blown apart by the resulting explosion, and went hurtling outwards, condensing into the great galactic systems of stars which fill all observable space almost uniformly. The astronomical observation that distant galaxies are receding from us, at velocities which increase uniformly with their distance, gave rise to the concept of the expanding universe, which would be a natural result of the initial explosion of a super-condensation of matter. It is believed that at distances great enough for the galaxies populating that part of space to be moving away with the velocity of light, they would disappear from our ken, thus providing a limit to the size of the universe as we could know it. It is assumed also that the energy available to keep the stars which constitute the galaxies hot and luminous is gradually used up as the hydrogen becomes converted to heavier elements, and that cold, dark inertness will inevitably be the final state of all matter. This evolutionary picture of birth, life and death of the universe ignores the problem of the origin of the hydrogen which was the primordial substance.

Such cosmological ideas have been challenged with considerable success of recent years by Hoyle, Gold and Bondi. These ingenious theoretical astronomers believe that the universe may, in fact, be static as a whole, an unchanging general distribution of matter being preserved throughout space. Since observation shows that the universe is expanding, they preserve constant concentration of matter in space by postulating the continuous creation of matter, as hydrogen atoms, at a constant rate in every part of space. They dispose of the argument that such spontaneous appearance of hydrogen atoms has never been observed, by pointing out that the rate of birth of new atoms required to maintain a static universe is so slow that it would be surprising if it had been observed. The universe has existed for all time and will continue to exist for evermore. Wherever he was located in space, an observer would see exactly the same universe as he sees from the earth. "As it was in the beginning, is now, and ever shall be, world without end."

These newer ideas dispose of many of the difficulties of the origin of the universe as a single gigantic explosion which took place about ten thousand million years ago. However, they introduce continuous creation, with no hint of a source of the enormous energy which would be required, on current ideas, to create the new hydrogen atoms. This difficulty is overcome by the bold hypothesis that conservation of mass-energy is not universally valid, and that continuous creation is a natural property of space. If Hoyle, Bondi and Gold are correct, there must be a severe overhaul of many of the cherished ideas of science. Tests to determine whether the static picture is correct have been devised and are under way. So far no one has been able to demonstrate that continuous creation does not take place, or that the observable universe is not in accord with this revolutionary theory, in which both time and space stretch to infinity in all directions.

The answer to many of these intriguing problems, which are so important for the fundamentals of science and philosophy, may emerge from the endeavours of theoretical physicists to produce a unified theory which, by one set of postulates, will explain all that we know of matter. The quantum theory and the theory of relativity have together achieved a satisfying picture of matter and its interactions with light and other electromagnetic radiation. However, no success has been achieved in bringing into the picture that universal property of matter, gravitational attraction. Physicists await the emergence of a unified field theory, as it is called, with great curiosity and impatience. Perhaps, when it does come, it will result in changes in our ideas as revolutionary as those produced by the quantum theory and the concepts of relativity.

We have seen how the Victorian ideas of certainty and causality in science have been replaced by uncertainty and indeterminism. Ideas have been born which bear no relation to everyday experience, but which are now an accepted part of the concepts of science. The senses prove to be a poor guide to reality. As physical science has made this revolutionary change in its concepts, it has, strangely enough, become far more powerful in its approach to all problems which face it. Nevertheless, the lesson has been learnt and the smug certainty of the past has gone. The boundless wonder of the physical world fills the man of science with humility, but drives him to discover more and more about it. He no longer expects to find a final answer to any question. His hope is that he may be able to formulate better and better approximations to a description of reality.

IPRONIAZID ("MARSILID") IN THE TREATMENT OF DEPRESSION.[1]

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IN any assessment of a new drug, results based on a statistically designed experiment are always desirable in contradistinction to those based on clinical observation and impressions. In psychiatric practice, the difficulties are further increased by the inability to assess adequately the possible placebo effect of the drug used, the personality of the therapist, the enthusiasm or scepticism with which the therapist uses the drug, and the effects of the psychotherapy, brief and superficial though this may be, that are inseparable from the psychiatrist-patient relationship. This paper suffers from all these defects. It is based on impressions gained in the treatment of patients in private psychiatric practice. Figures are quoted which seem to support the impressions. However, it is freely accepted that a more carefully controlled study will be necessary before the impressions here expressed can be accepted as valid.

Iproniazid ("Marsilid") is an inhibitor of monoamine oxidase, an enzyme widely distributed in the central nervous system. It has the ability, therefore, to prevent the breakdown of serotonin by this enzyme. This is thought to underlie its use in the treatment of depressive states in man.

Serotonin.

Page (1957) points out that vasoconstrictor substances had been observed in the serum of normal people and animals almost 100 years ago. In 1947, he and his co-workers suggested that this vasoconstrictor substance was closely related to tryptamine, and gave it the name serotonin. The final structure was determined by Rapport (1949), who showed it to be 5-hydroxy-tryptamine. Page writes that the discovery in 1952 that serotonin was present in relatively large quantities in the brain came as a genuine surprise. At about the same time, Amin, Crawford and Gaddum (1954) also found that the brain contained more than its fair share of serotonin, and demonstrated that its distribution closely followed that of noradrenaline. The highest concentrations were in tissues associated with the central autonomic representation.

Udenfriend, Weissbach and Bogdanski (1957) point out that the serotonin in the brain is not randomly distributed, but is localized in definite areas. Thus, the primitive portions of the brain, such as the hypothalamus and mid-brain, contain relatively large amounts. The cortex and cerebellum contain very little. The enzymes, 5–hydroxytryptophane decarboxylase, which makes serotonin, and monoamine oxidase, which metabolizes it, are also widely distributed in the brain, but show highest concentrations in the hypothalamus. In view of the fact that the hypothalamic region is closely under scrutiny in its relation to mental and emotional disorders, the significance of these discoveries on the distribution of serotonin cannot be under-estimated.

The Significance of Serotonin.

Marrazzi (1957) draws attention to the structural chemical similarities between adrenaline (epinephrine), amphetamine and mescaline on the one hand, and adrenochrome, D-lysergic acid diethylamide (LSD–25) and serotonin on the other. He points out that mescaline, LSD–25 and adrenochrome all have the ability, when given to human volunteers, of producing a full-blown "model psychosis". Working on cats, Marrazzi was able to show that mescaline, LSD–25 and serotonin all produced synaptic inhibition identical in kind to that produced by adrenaline. Serotonin turned out to be the most effective cerebral synaptic inhibitor of all.

Woolley and Shaw (1957) discuss their idea, first presented in 1954, that serotonin has an effect on the pulsations of oligodendroglia. Serotonin has been observed to cause these cells to contract strongly. If an antimetabolite of serotonin is added, the cells are restored to their normal slow, pulsating, rhythmical contractions. On the basis of these observations, Woolley and Shaw suggest a possible function of serotonin. They point out that the brain is poorly vascularized in comparison with organs such as the kidney, and this has led to the belief that the oligodendroglia are little stirring devices designed to facilitate circulation of extravascular fluid. An excess of serotonin could stop this stirring action by causing tetanic contraction of the cells. On the other hand, a deficiency of serotonin could slow down the normal pulsations. In both cases, the normal supply of nutrients and the removal of waste products are impeded.

In this connexion, the relation of reserpine to serotonin is of some interest. Shore and his co-workers (1957) assemble data to show that the primary action of reserpine is to release serotonin from its various binding sites including those in the brain. The released serotonin is then metabolized by monoamine oxidase. The serotonin that continues to be made presents a persistent low concentration of free serotonin to brain tissue. These authors attribute the action exerted by reserpine to this free serotonin.

Brodie and Shore (1957) showed that the effects on rabbits of reserpine alone and reserpine after pre-treatment with iproniazid were markedly different. In the latter case, the animals, instead of showing the usual sedative effect of reserpine, were now excited. Iproniazid given alone, while it prevented the breakdown of serotonin, produced no overt effect. Excitement occurred when the reserpine had released additional serotonin from its depots, leading to excess of free serotonin. The effect was just the opposite of that observed when reserpine was given alone.

On the basis of these observations, it is suggested that reserpine is effective in excited states by releasing serotonin from the brain and speeding its metabolism by monoamine oxidase. The resultant lowering of the content of free serotonin leads to sedation. On the other hand, it is known that reserpine can induce a deep depression in certain individuals. In a recent paper, Ayd (1958) presents evidence that this occurs only in obsessive personalities, with a predisposition to or a previous history of depressive episodes. At least, it is suggestive evidence that depressive states may be associated with a low free serotonin content. On the basis of this hypothesis, one could argue that depressive states could be relieved by increasing the amount of free serotonin by preventing its breakdown. This can be achieved by inhibiting the metabolic action of monoamine oxidase with iproniazid.

In this connexion, it may be mentioned that Udenfriend *et alii* (1957) produced an excited state in rabbits by giving large doses of 5–hydroxytryptophane. This substance is decarboxylated to serotonin. The resultant high concentration of serotonin presumably saturates the binding sites and gives rise to an excess of free amine.

Iproniazid ("Marsilid").

In discussing the history of "Marsilid", Davis (1958) points out that isoniazid and iproniazid were synthesized about the same time in 1951 for the treatment of tuberculosis. Clinical trials showed that, in the doses used for tuberculosis, iproniazid was more toxic than isoniazid, and the former was nearly abandoned. It is of interest that central nervous stimulation was listed as one of the undesirable side effects. Bosworth (1958) records that he had to convince Hoffman-La Roche to continue production of "Marsilid", for he believed the drug was not only effective in the treatment of various infections, but also that it helped the patient in general and the healing process in particular.

An early report of Kamman, Freeman and Lucero (1953) on the use of iproniazid in the treatment of

[1] Paper presented at the annual meeting of the Australasian Association of Psychiatrists, held in Perth, Western Australia, from October 13 to 16, 1958.

long-term mental patients was not encouraging, though the authors concluded it had a certain small positive effect. However, later reports were more enthusiastic. Crane published two papers in 1956 on the use of iproniazid in debilitated tuberculous patients. Though he encountered a high toxicity rate, because of the large doses, from 300 to 450 mg. per day, he nevertheless concluded that the greatest value of the drug lay in its ability to create a sustained feeling of vitality and well-being in debilitated and depressed patients. He believed this effect was unsurpassed by any other drug. Scherbel (1957) treated patients with rheumatoid arthritis, and was impressed with the improvement in mood and the gain in weight, even though he could not accept that the drug had any beneficial effect on the arthritic process. In the same year, Kline (1957) reported on the results of treatment of severely depressed and regressed psychotic patients in hospital. Although not all the patients were improved, and in some cases the improvement came very slowly, the point was made that iproniazid had helped some chronically depressed patients who had not been helped by any other therapy. In a more recent paper on his clinical impressions, Kline (1958) comes out enthusiastically in support of its efficacy in cases of depressed and lethargic patients seen in his private practice. He reports success in the treatment of patients with obsessions and raises the question, on this result, whether or not there may be depression underlying most cases of obsession. It is not without significance that depression occurs frequently in persons with an obsessive personality make-up. All authors agree that toxic effects can occur in treatment. De Verteuil and Lehmann (1958) were so alarmed by the frequency of undesirable and serious side effects in their small sample that they discontinued the use of the drug. However, this appears an unnecessarily cautious attitude, as other authors have shown that side effects do not cause concern if the dosage is carefully controlled. This is the writer's experience.

Mode of Action of Iproniazid.

As has been pointed out, iproniazid inhibits the action of the enzyme, monoamine oxidase. This enzyme metabolizes serotonin. However, it can also metabolize other amines, and the question arises whether it also is associated in the breakdown of noradrenaline and adrenaline. Shore (1958) gives experimental evidence to suggest that iproniazid does in fact cause a rise in both brain serotonin and noradrenaline. This author finds it difficult to state whether the increase in serotonin or in noradrenaline is of the greater importance in the central effects of iproniazid. However, Resnick *et alii* (1958) throw some doubt on the effects on noradrenaline metabolism. They conclude that iproniazid treatment in man clearly inhibits the action of monoamine oxidase, but does not influence those enzymes responsible for the O-methylation of adrenaline. Of course, it is still open to question whether, in fact, iproniazid acts by its effects on brain serotonin and/or noradrenaline levels, or by some other means not yet determined.

Dosage and Side Effects.

Crane (1956*a*) found the use of iproniazid in high dosage limited by the frequency and severity of side effects—twitching of the lower extremities, vertigo, ataxia, urinary spasms, constipation, hyperreflexia, drowsiness, insomnia, dryness of the mouth, and symptoms caused by cardiovascular insufficiency, anæmia and liver damage.

Scherbel (1957), using smaller doses, 150 mg. per day initially, encountered the following side effects: constipation, loss of libido, lightheadedness, postural hypotension, blurring of vision, hyperactivity of deep reflexes and clonus. Jaundice did occur, but only in patients with a history of previous liver disease. He was not alarmed by them and found they responded to reduction in dosage or cessation of treatment. Kline (1958) points out that, like with any potent drug, inevitably there are side effects, of which jaundice is probably the most serious. In the series of 31 cases reported by de Verteuil and Lehmann (1958), one patient sustained a fracture of the tibia in a fall due to ataxia, and another died from acute toxic necrosis of the liver. Peripheral neuritis may occur with tingling and paræsthesia of the limbs, followed by weakness and paralysis of muscle with loss of deep reflexes. Pyridoxine can largely prevent the development of this complication. Psychotic episodes or epileptiform fits are occasionally encountered, usually in patients with a history of epilepsy or of previous psychotic illness.

The author has encountered side effects in the cases presented; in fact the dose has mostly been maintained at the initial level until side effects have supervened. However, he has never been troubled by them. The commonest side-effect encountered has been a sense of dizziness or swaying. Other patients have complained of pains in muscles and some tendency to involuntary jerks. Two males noticed impotence. Constipation has never been really troublesome. Swelling of the ankles has been noted, and a difficulty in initiating the act of micturition. Insomnia has occurred, but is relieved by dropping the dose and giving it in the early part of the day. One hysterical patient complained of severe ataxia, but it was difficult to determine if, in fact, the symptom was due to the drug. There appears to be a tremendous individual variation in tolerance to the drug. For example, one woman took 200 mg. per day for five weeks without developing side effects. Another man suffered a relapse of symptoms when the dose was reduced from 150 mg. to 100 mg. per day, because of his improvement; he had never shown any side effect. On the other hand, some patients will continue to experience mild side effects on 50 mg. per day.

Scherbel (1957) and Kline (1958) both emphasize the need to reduce dosage drastically as soon as improvement occurs or at the onset of toxic symptoms. The latter recommends that treatment should be commenced with 50 mg. three times a day. In acute depression he also gives 10 to 30 mg. of amphetamine initially. He advises that the patient should be warned of possible side effects, but unless these are marked the dose should be continued until there is a therapeutic response. Treatment with lower doses takes much longer or is not effective at times. As soon as evidence of therapeutic response has been obtained, the dosage should be dropped to between 10 and 25 mg. per day and continued for one week. If symptoms recur the dosage should be lowered until a maintenance level is established. After one or two months, a further trial may be made to reduce the dosage level.

The writer commences treatment with 50 mg. three times a day. At the onset of side effects, the dose is at once dropped to 50 mg. in the morning and 25 mg. at midday. A further reduction to 25 to 50 mg. each morning may be necessary. In cases in which improvement occurs in the absence of side effects, the tendency has been to reduce the dosage less markedly to 50 mg. morning and midday.

Some patients show a relapse of symptoms, and need a temporary increase in dose. Later the dosage can often be reduced without any return of symptoms. Kline (1958) comments that his patients manifest an anomaly, in that some of the patients require maintenance doses and others do not. This has been the writer's experience.

The Present Investigation.

The present preliminary investigation was started after two patients with a long history of melancholia and much treatment by electroconvulsive therapy without lasting benefit appeared to respond to iproniazid.

One patient had been ill for six months and had had 21 sessions of electroconvulsive therapy in this time. When put on iproniazid, 200 mg. per day, she responded after a further two sessions of electroconvulsive therapy, and had kept well.

Another patient had been ill for 11 months, and been treated by 33 sessions of electroconvulsive therapy and also

a course of full-coma insulin (because of her failure to respond and certain schizophrenic features) before being started on iproniazid, 150 mg. per day. She showed steady progress in the next 14 days, and could be discharged from hospital, better than she had been for over a year.

This type of response encouraged the writer to use this drug more widely. This paper presents 46 cases treated with iproniazid alone or combined with electroconvulsive therapy (Table I). As will be seen, the

TABLE I.
Treatment and Results in 46 Cases.

Diagnosis.	Method of Treatment.	No. of Cases.	Results.		
			Much Improved.	Improved.	Unchanged or Worse.
Endogenous depression.	Marsilid *plus* electroconvulsive therapy:				
	In-patient ..	17	16	1	—
	Out-patient ..	5	4	1	—
	Marsilid	6	6	—	—
Neurosis:					
Anxiety neurosis with depression.	Marsilid	7	2	4	1
Anxiety hysteria with depression:					
In-patient	Marsilid *plus* electroconvulsive therapy.	3	—	—	3
Out-patient	Marsilid	6	—	—	6
Depression: cancer of œsophagus.	Marsilid	1	—	—	1
Depression: cerebral tumour.	Marsilid	1	—	1	—
Total ..	.. .. ..	46	28	7	11

patients who responded best were those suffering from endogenous depression. Cases of anxiety neurosis with depressive features responded less well, while anxiety hysterics, with pseudo-depression, did poorly. These results compare with those reported in a series of 131 cases by Dally (1958). His best results were in cases of depression with weight loss — cases probably diagnosed in this series as endogenous depressions. Neurotic subjects did poorly.

As the investigation proceeded, the impression arose that patients treated by a combination of iproniazid and electroconvulsive therapy responded more quickly and required less electroconvulsive therapy than those treated by electroconvulsive therapy alone. Whether the cases so treated would have responded to iproniazid alone is outside the scope of this paper. Robie (1958) believes that iproniazid may replace electroshock therapy, and recommends it should be given a four-weeks trial. However, it is uneconomic to keep the patient in a private hospital waiting for four weeks to see if the drug alone will produce a remission or an improvement. It was for this reason the combined therapy was adopted.

Admittedly, the author has had experience of several patients responding to iproniazid when they had failed to improve on other methods of treatment. Also, several of the six patients listed in the table under "endogenous depression", who had iproniazid alone, had previously had electroconvulsive therapy either for previous attacks of depression or earlier in the present illness, and responded equally well or even better to the drug.

It was decided to test the impression that endogenous depression responds in a shorter time and with fewer sessions of electroconvulsive therapy when iproniazid is combined with this therapy, by comparing a series of patients so treated with a random selection of patients from the writer's files treated by electroconvulsive therapy alone. Seventeen patients comprise the first series; 30 patients are listed as controls. Of the controls, two patients had had three separate endogenous depressions in the period 1951 to 1958 covered by the case histories chosen. So that all cases would be comparable, only the first admission to hospital of each of the two patients was considered.

The length of stay in hospital is an imperfect measure of the effectiveness of a therapy. Admittedly, patients vary greatly in their response to any form of treatment, and this is so with electroconvulsive therapy. Nevertheless, it was decided to use the number of days spent in hospital as a measure of therapeutic efficacy.

Results.

The results of this investigation are presented in Figures I and II. Of the 17 patients treated by iproni-

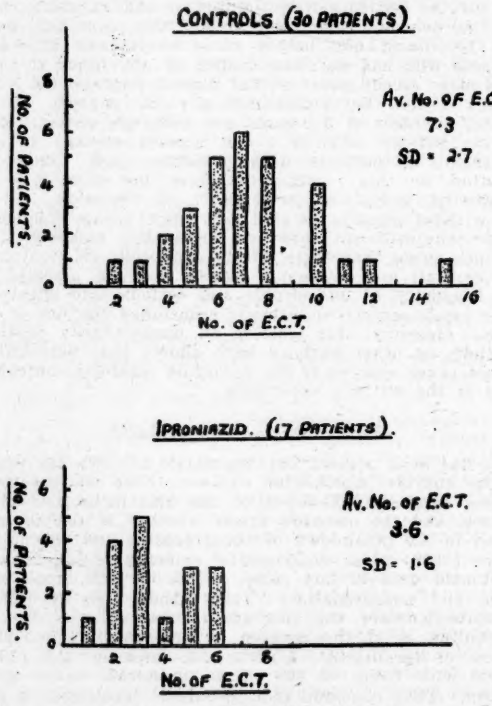

FIGURE I.

azid and electroconvulsive therapy, the number of sessions of electroconvulsive therapy required varied from 1 to 6, with a mean of 3·6, and a standard deviation of 1·6. Of the 30 patients used as controls, the number of sessions of electroconvulsive therapy had a range of 2 to 15, with a mean of 7·3, and a standard deviation of 2·7. The time spent in hospital by the 17 patients treated by iproniazid and electroconvulsive therapy, varied from 6 to 32 days, with a mean of 20·4 days, and a standard deviation of 7·6. An examination of the records of the 30 controls showed that the period in hospital ranged from 10 to 81 days, with a mean of 36·6, and a standard deviation of 19·5.

As there was a significant difference in the variances, the non-parametric median test was used to assess the significance of the observed difference between the two sample distributions. For the number of sessions of electroconvulsive therapy used in the two samples, this test gave a χ^2 value of 13·0 and an associated probability of less than 0·001. This is highly significant. For the number of days spent in hospital, the median test gave a χ^2 value of 5·7 and an associated probability of less than 0·02. Here again there is a significant difference.

Follow-Up Studies.

Sixteen patients in the iproniazid and electroconvulsive therapy group could be followed up. The period since discharge from hospital varied between six weeks and six months. Two patients had definitely relapsed. The remainder were well. Seven patients had stopped taking iproniazid without return of symptoms; seven were taking a maintenance dose varying from 25 to 50 mg. each morning.

Conclusions.

The writer has no doubt that iproniazid used in conjunction with electroconvulsive therapy definitely shortens the period of treatment in endogenous depressions, and reduces significantly the number of sessions of electroconvulsive therapy required. The figures presented support this view. Whether iproniazid alone would be as effective the writer cannot say. Robie (1958) suggests that it is, and advises a month's trial. In milder cases, the writer has used the drug alone with benefit. However, the results with the combined treatment are so good that it is recommended that this method be used for sick patients requiring admission to hospital.

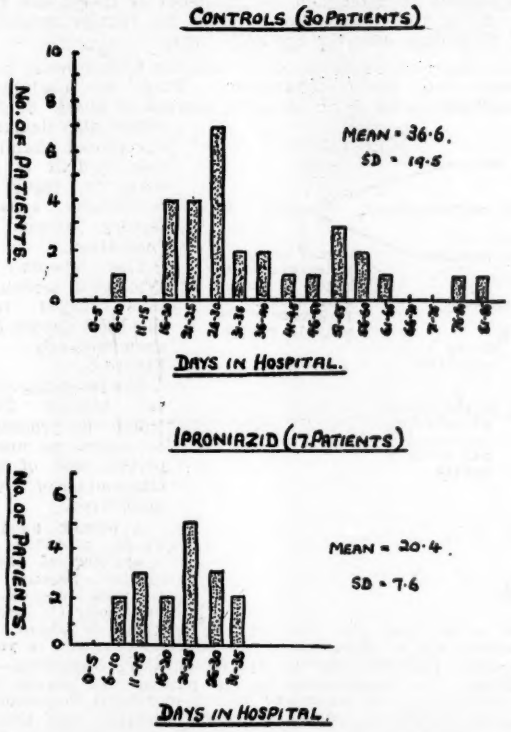

FIGURE II.

There is an impression, but an impression only, that, in some patients at least, the quality of the improvement from the combined therapy is better than that from electroconvulsive therapy alone. Three patients in the series had been treated before with electroconvulsive therapy with a degree of improvement that was definitely inferior to that achieved by the use of iproniazid with electroconvulsive therapy.

Kline (1958) suggests that it may be necessary to revise our concept of obsessions, pointing out the possibility, as a result of his experience with iproniazid, that depression may be a hidden factor in patients with obsessions. From his experience, the writer believes that the diagnosis of depressive states must be made more accurately. From his review of the 46 cases, presented in Table I, he is convinced that iproniazid is most effective in those cases in which the mood change is accompanied by alteration in both the mental and physical state, that is, in true endogenous depression. There must be present not only depression, loss of interest, inability to concentrate, forgetfulness and insomnia, but also anorexia, a furred tongue, a significant loss of weight and possibly constipation. The depression is almost invariably worse in the mornings, and the insomnia is found significantly in the early hours of the morning. The large majority of patients have obsessive personalities. In cases in which these criteria are not fulfilled, the results of iproniazid therapy would appear to be far less encouraging. Further controlled clinical trials will be necessary to clarify this point.

Iproniazid is a safe drug as long as it is carefully controlled. Side effects are minimal and cause little worry if the dose is reduced as soon as side effects appear. However, it must be remembered that it is a potent and toxic drug, and could be dangerous in inexperienced or incautious hands.

The beneficial effects of iproniazid strongly suggest that endogenous depression is a biochemical disorder of the central nervous system involving the hypothalamus.

Acknowledgements.

The writer desires to express his thanks to Mr. S. H. Lovibond, Department of Psychology, University of Adelaide, for analysing the results and providing the statistical evaluation incorporated in this paper.

Grateful thanks are extended to Roche Products Ltd., Sydney, for a liberal supply of "Marsilid" tablets.

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CYTOLOGICAL DETECTION OF UNSUSPECTED CARCINOMA OF THE CERVIX.

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As information accumulates, it is becoming more and more apparent that exfoliative cytology is a reasonably reliable procedure for the early and accurate diagnosis of the commonest malignant tumour in women—cervical carcinoma. Indeed, it has been the consensus of opinion at the five cancer conferences sponsored by the United States Public Health Service that cytological screening ought to be performed regularly on all women over the age of 30 years.

The increase in the number of new cases discovered has been to a large extent in the category of carcinoma-in-situ, and most of these are quite unsuspected clinically. As a matter of fact, gynæcologists are frequently unable to localize the in-situ lesion even when the smear finding has been reported as positive. For this reason, the clinician often finds it necessary to make punch biopsies at several places in the circumference of the cervix to confirm the presence of carcinoma-in-situ. Such biopsy confirmation is, of course, always essential, since even a positive report on the smear examination should be regarded as only presumptive evidence of carcinoma and indicates the need for further investigation.

It is not uncommon for carcinoma-in-situ to be found in only one of many punch biopsies representative of different areas in the circumference of the cervix. If in-situ rather than invasive carcinoma is found in any of these blocks, a cold knife conization of the cervix should then be carried out in order to exclude the presence of invasive tumour elsewhere, since the treatment of these two conditions is radically different. The doughnut-shaped ring of tissue removed by conization is cut into sections circumferentially as one would cut a cake into segments, and these multiple blocks are examined microscopically. Unless invasive tumour is found in one of the preliminary punch biopsies, examination of a total circumferential cone becomes imperative.

Papanicolaou smears are taken under direct vision by scraping the cervical os with a wooden disposable Ayre's spatula. Films are made and immediately fixed while wet in an ethanol-ether mixture. As a routine, two smears are made and dropped back to back into a suitable wide-necked bottle containing fixative. The smears are scanned by specially trained cytological technicians, who will mark any suspicious cell or clump of cells with Indian ink. This marking is done conventionally, with the identification label of the slide to the left of the mechanical stage and the ink dot placed to the right of the cell clump with the right hand. When the slides are viewed microscopically, the image is reversed and the ink dot appears to the left of the suspicious cells. In order not to disturb cells during the marking, the stained and mounted slides are heated on a hotplate until the balsam is quite hard. The pathologist can then easily identify the suspicious cell groups and make the final report.

There are several ways of reporting on Papanicolaou smears. Some centres use grades or numbers, but perhaps the simplest method is to use one of the following four categories: (i) positive, (ii) negative, (iii) inconclusive, (iv) unsatisfactory.

Additional space should also be provided on the report for a short comment on the smear. An inconclusive report means, in effect, that abnormal cells have been found, and always demands preparation and examination of further smears. However, the degree of abnormality is a subjective determination, and the report may be accompanied by a suitable comment—for example: "Highly suspicious: please biopsy and repeat smears." The more experienced the cytologist, the fewer false positive and inconclusive findings will be reported. On the other hand, false negative findings must undoubtedly occur; but it is impossible to determine the incidence of these, and this is one of the reasons for advising the regular screening of all women over the age of 30 years.

A report of "unsatisfactory" signifies a technically poor smear—too thick, inadequately fixed, or containing insufficient cells or an excessive amount of blood. Such a report also demands a repeated examination, and it is not wise to report a technically unsatisfactory smear as "negative".

The schema for cytological screening thus should take the lines shown diagrammatically in Figure I.

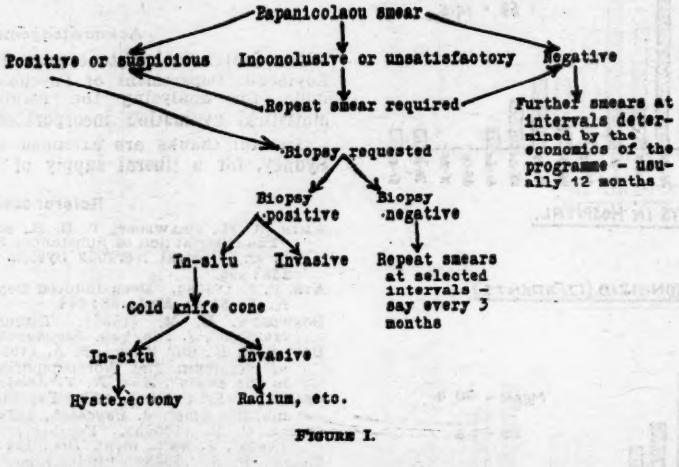


FIGURE I.

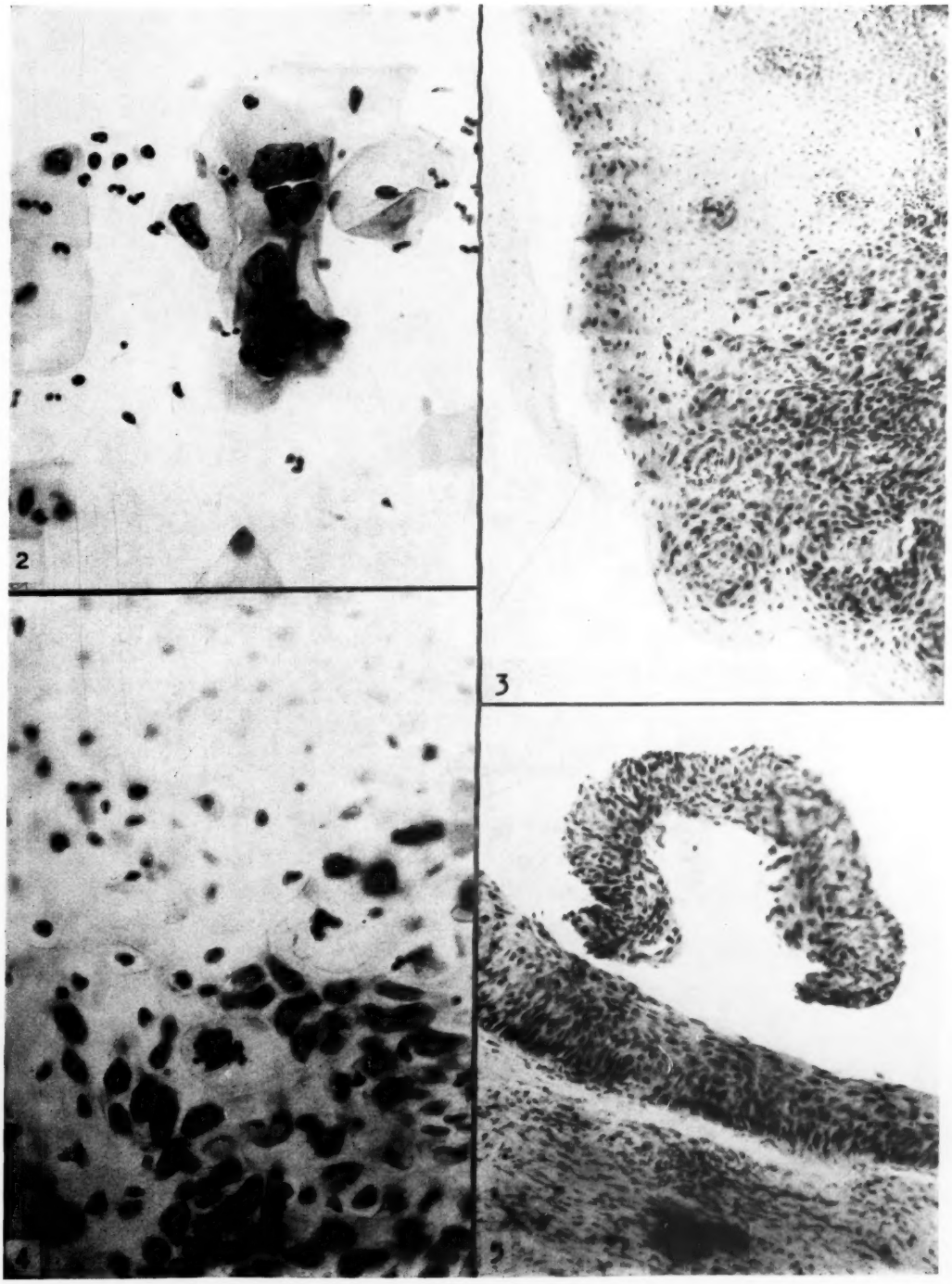
The following clinical history illustrates the procedure by which an unsuspected case of carcinoma-in-situ was discovered.

A woman, aged 37 years, attended for gynæcological examination because of a mild degree of cystocele. (It should be noted that the age of this patient is about the average age of incidence of carcinoma-in-situ, and 10 years younger than the average age for invasive carcinoma—48 years.) On examination of the patient, the cervix was described as pink, clean and healthy-looking. A Papanicolaou smear was prepared as a routine measure and showed malignant cells (Figure II), and the finding was reported as positive. The attending gynæcologist was unable to detect any lesion of the cervix, and so was in some difficulty in deciding which areas of the cervix to select for biopsy. Seven punch biopsies were made at random from the circumference of the cervix, and in only one of these was carcinoma-in-situ found (Figures III and IV). After these findings, conization should have been performed but was not, and instead a total hysterectomy was performed. When the whole of the cervix was cut into sections, carcinoma-in-situ was found in a further three out of ten blocks. But for the routine preparation of Papanicolaou smears this lesion would not have been detected, and such an experience is by no means uncommon.

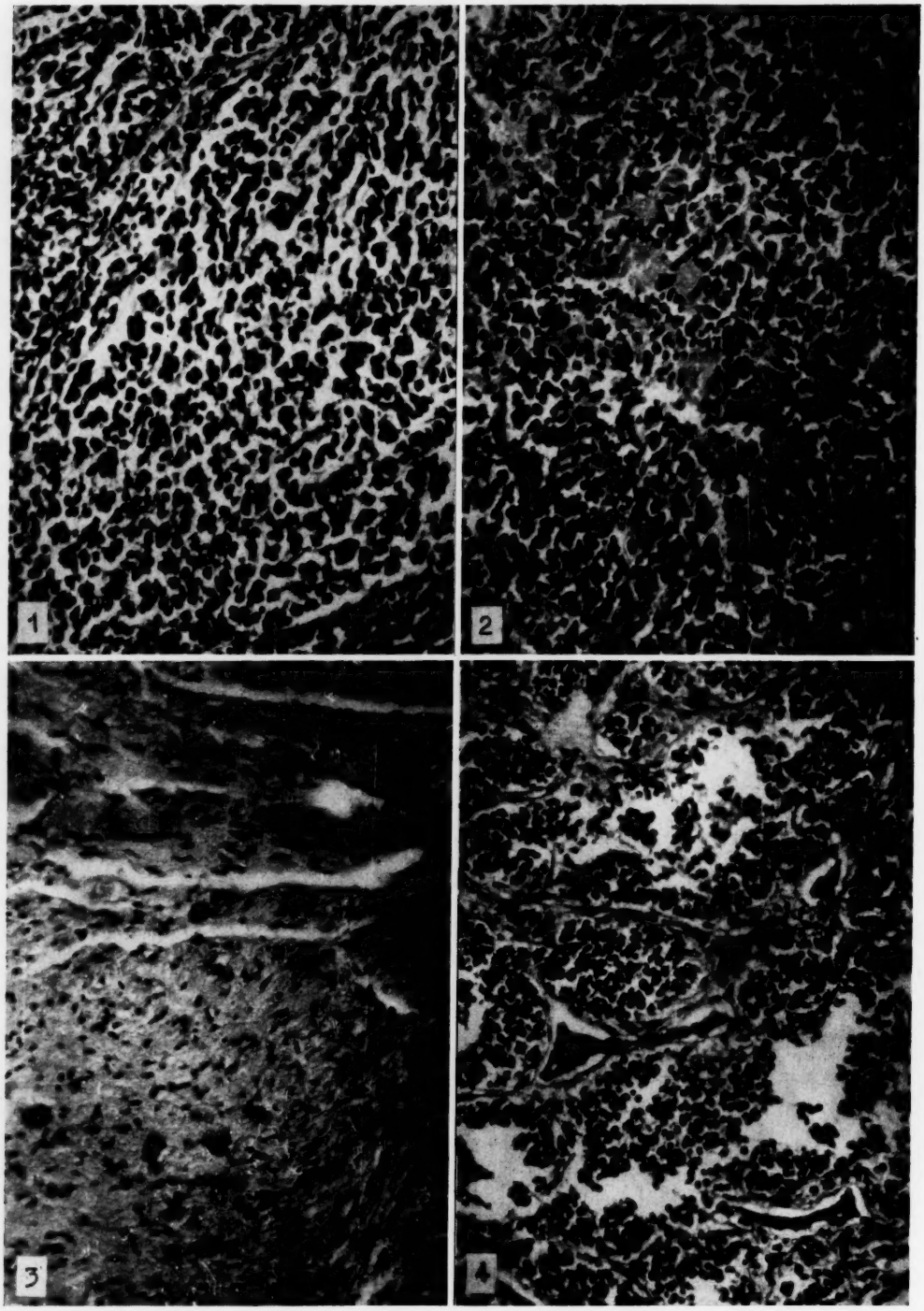
While the question remains unsolved as to whether carcinoma-in-situ, such as was found in the foregoing instance, is able to undergo spontaneous healing, it would be unsafe not to assume that it is always potentially invasive, even if on histological grounds alone. It is difficult to believe that epithelium such as that illustrated in Figures III and IV would not lead to progressive neoplasia with invasion if given sufficient time.

The possibility of spontaneous healing has not yet been substantiated, although it has been suggested that such healing may occur in some people. Just which case in particular will have this happy outcome, or what the

ILLUSTRATIONS TO THE ARTICLE BY C. E. MARSHALL.



ILLUSTRATIONS TO THE ARTICLE BY JOHN MURPHY.



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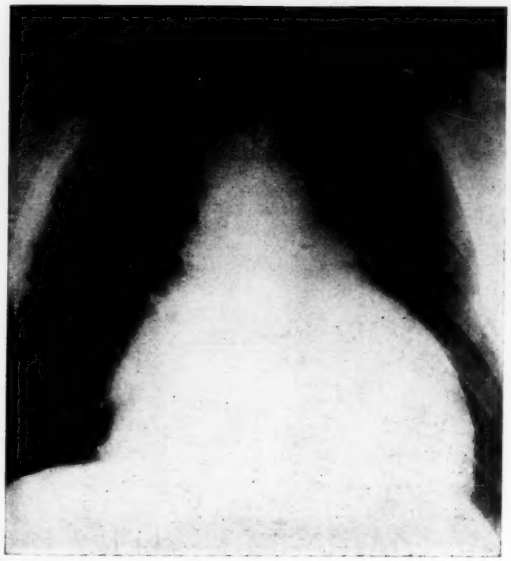


FIGURE I.

FIGURE II.

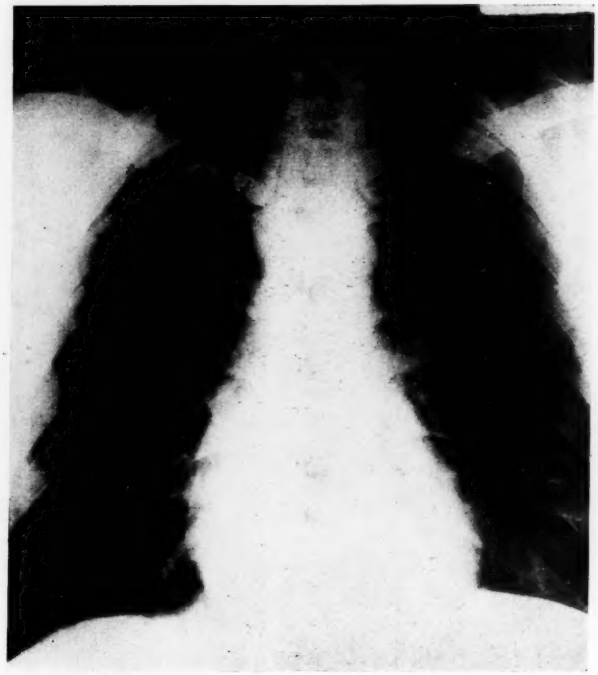


FIGURE III.

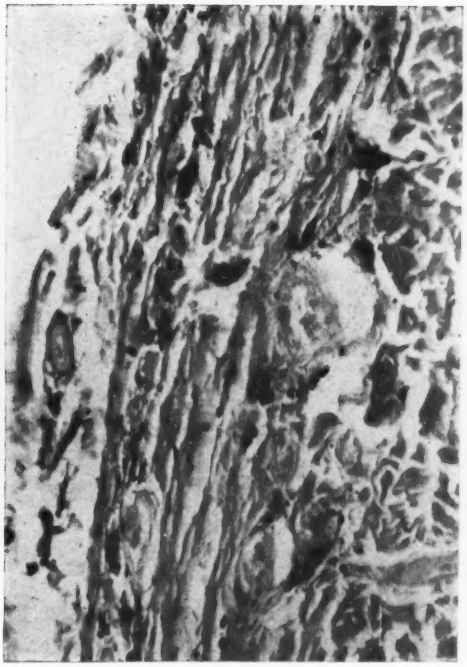


FIGURE VII.

ILLUSTRATIONS TO THE ARTICLE BY G. S. SANTOW.

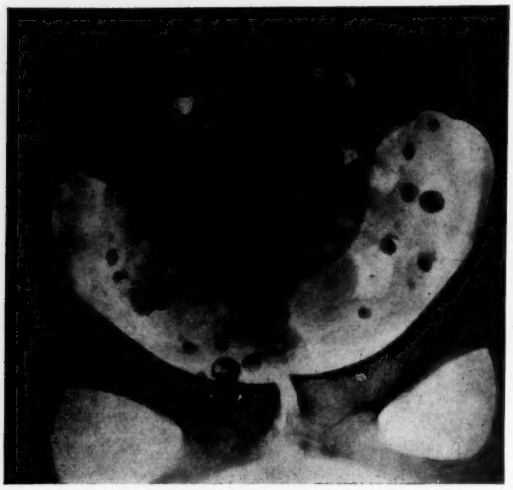
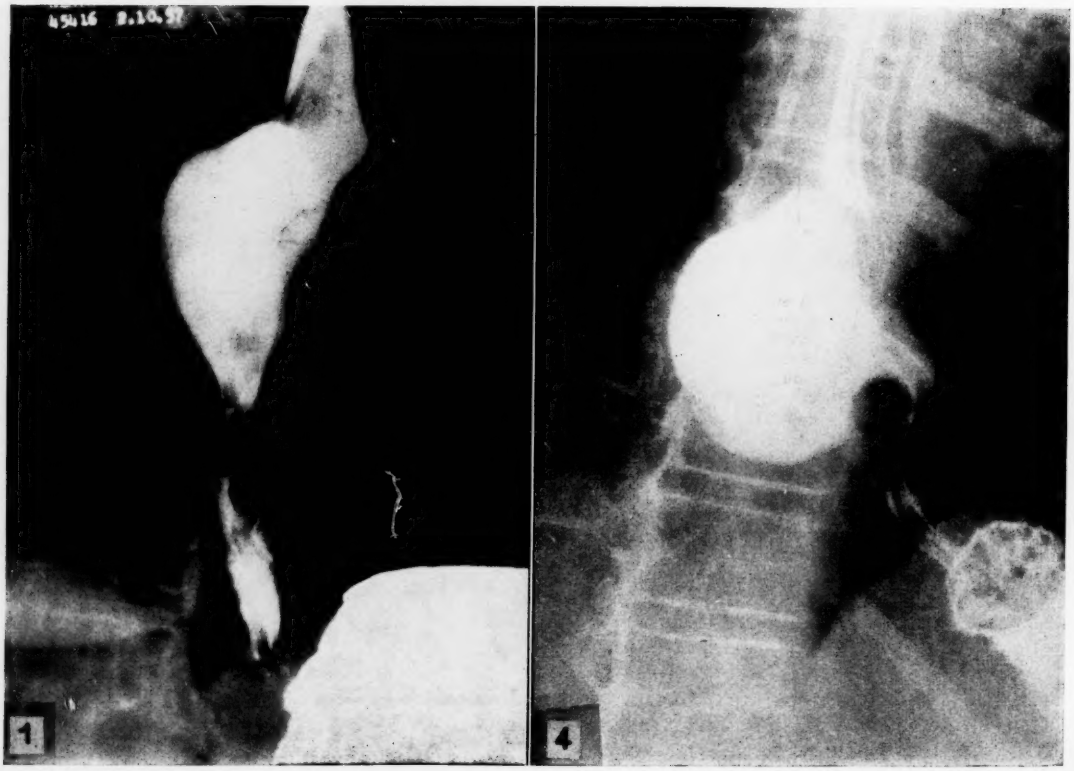


FIGURE II.

ILLUSTRATIONS TO THE ARTICLE BY GORDON CHAMBERS.



mechanism of such hypothetical healing may be, it is as yet impossible to say.

As a speculative observation, it is often found in biopsies of cervices showing carcinoma-in-situ, that there occur strips of histologically malignant epithelium lying curled up and separated from the stroma, much as if they had become peeled off the connective tissue like a strip of adhesive tape (Figure V). At what stage between biopsy and the cutting of the sections this happens is not clear; but it does show the readiness with which the malignant epithelium can become stripped off the underlying connective tissue. Cleavage appears to take place along planes of a submucosal capillary network; but such peeling does not occur with invasive carcinoma, in which the tumour is too intimately mingled with the connective tissue for this to be possible. Since more cases of carcinoma-in-situ than of invasive tumour are discovered, it is possible that in some cases in which the in-situ change is limited, spontaneous cure may be brought about in this manner by exfoliation of unhealthy epithelium. In other cases cure may be unwittingly effected by the biopsy itself; but it would not be safe to suggest at the present stage of our knowledge that conization is in itself a cure. (We have on record a case in which repeated positive findings from Papanicolaou smears were obtained three years after a complete conization in which the tissue showed carcinoma-in-situ. No visible lesion had appeared in the cervix during these three years, although malignant cells still continued to exfoliate.) In still other cases, carcinoma-in-situ may progress to invasive carcinoma in the course of 10 years or so. In some centres, treatment is being deliberately withheld from patients with carcinoma-in-situ and positive smear findings but no visible lesion. This is being done in order to find out what is the natural history of carcinoma-in-situ.

During a period of 15 months following the initiation of a cytological screening service, smears from 4919 women were examined. The findings in 23 smears were reported to be "positive" or "suspicious", and the patients were confirmed by biopsy as having carcinoma of the cervix. (Additional smears showing atypical cells, but not confirmed as carcinoma, and cases of endometrial hyperplasia and endometrial carcinoma and a case each of mixed mesenchymal tumour and cervical fibroid tumour in which abnormal-looking cells were shed, have not been included in this series.) The 23 confirmed cases represent a yield of 0·47%, and this is about the mean of the national figures, the lowest being about 0·3% and the highest about 0·7%.

The most interesting aspect of these discovered cases of cervical carcinoma is that 14 were cases of carcinoma-in-situ (patients' average age 41 years) and nine were of invasive carcinoma (patients' average age 48 years). There were thus one and a half times as many in-situ as invasive lesions. Of the 14 patients with carcinoma-in-situ, only two had any visible lesion on the cervix, and the remaining 12 cases were quite unsuspected by the clinician until he received the Papanicolaou report. Of the nine patients with invasive carcinoma, however, only three were without symptoms or signs, and they were investigated for other reasons, such as examination for insurance, cancerophobia following a sister's death from cervical carcinoma, and cancer publicity. These findings demonstrate beyond doubt the value of the cytological smear in discovering cervical carcinoma while it is still in its pre-invasive stage, and the figures and illustrations are offered in the hope that more people may be converted to the use of the technique when facilities become available for the adequate training of responsible technicians. In the United States, the procedure is held to be so vital that all pathologists are being urged to agree upon a low and uniform fee for smear examinations, so that any woman who desires the test may have it performed without feeling that it is a financial hardship.

Legends to Illustrations.

FIGURE II.

Papanicolaou smear from a patient with carcinoma-in-situ of the cervix, showing a group of malignant cells. The nuclei are large and hyperchromatic compared with a few normal cells, which are also present. (High power of the microscope.)

FIGURE III.

Biopsy section from a patient with carcinoma-in-situ of the cervix (same case as Figure I). The darker malignant epithelium shows an abrupt transition to lighter benign epithelium. (Low power of the microscope.)

FIGURE IV.

High-power view of Figure III, showing transition zone between carcinoma-in-situ and normal epithelium. The transition is abrupt, and malignant and benign cells are lying contiguous to each other. The malignant epithelium contains cells with large hyperchromatic nuclei, and at least two malignant mitoses are visible.

FIGURE V.

Carcinoma-in-situ, showing a curled-up strip of exfoliated malignant epithelium. Adjacent to this there is a portion of the cervical mucosa, showing a further strip of malignant epithelium in process of cleavage from the underlying stroma. (Low power of the microscope.)

NEUROBLASTOMA IN CHILDHOOD.

By JOHN MURPHY,
Department of Pathology, Royal Children's Hospital, Melbourne.

TOWARDS the latter part of the nineteenth century the group of tumours now called neuroblastoma was often confused with round cell sarcoma or lymphosarcoma. The papers of Pepper (1901) and Hutchison (1907) referred to this group as a sarcoma of the adrenal gland and liver respectively. Their clinical descriptions gave rise to two syndromes, Hutchison's and Pepper's, which have persisted to this day in text-books of pædiatrics.

In 1910, J. H. Wright reviewed the earlier theories as to the origin of neuroblastoma. He refuted the arguments that these tumours arose from gliomatous tissue, and presented convincing evidence that the neuroblastoma was a tumour of embryonic sympathetic ganglion cells. His descriptions, both macroscopic and microscopic, conform with modern usage.

Herxheimer (1914) showed by silver impregnation methods that the fibrillary structures seen in neuroblastoma were neural in type.

In the present study, autopsies were performed on nine children who died of neuroblastoma in the Royal Children's Hospital, Melbourne, during the period 1950 to 1957. The following is a short review of the main clinical and pathological findings.

Clinical Findings.

Among the nine children were seven males and two females. The age at death varied from three months to four and a half years; four children died in the second year of life.

Either severe anæmia or progressive abdominal enlargement was the main presenting feature in seven of the nine cases.

Severe Anæmia.

Four children were admitted to hospital with the classical signs and symptoms of severe progressive anæmia. A provisional diagnosis of acute leukæmia was made in each case. The hæmoglobin level on admission ranged from 4·6 grammes to 7·5 grammes per 100 ml. of blood. The duration of symptoms before admission varied from one to three months. The anæmia in each case was normocytic in type; slight polychromasia, poikilocytosis, anisocytosis and hypochromia were present. There were no significant changes in the white cells, and in only one case were the platelets reduced in number. Bone marrow aspiration was performed on three patients, with a diagnosis of acute leukæmia being made in two and metastatic tumour in the other.

Persistent pains in the legs and joints, especially the hip, were prominent symptoms in three cases. The duration of the last symptom paralleled closely the duration of the anæmia. Bone tenderness was not mentioned in any of the cases.

Progressive Abdominal Enlargement.

Three patients presented with a history of progressive abdominal enlargement. In one case bilateral abdominal masses were noted at birth; these were situated in the upper part of the abdomen in the region of the liver and spleen. In two cases progressive abdominal enlargement had been present for two months and one month respectively. In both cases a mass was thought to be present in the liver. In no case was the enlargement attributed to an adrenal tumour.

A normochromic normocytic anæmia was present in all three cases; hæmoglobin levels ranged from 9·3 grammes to 12·8 grammes per 100 ml. of blood. However, signs and symptoms of anæmia, apart from pallor, were not marked.

Of the remaining two patients, one presented with a five months' history of recurrent bronchitis. The hæmoglobin value was 10·2 grammes per 100 ml. of blood, and at autopsy a mediastinal tumour was found. The other patient was admitted to hospital with a lump over the sacrum; the hæmoglobin value was 8·7 grammes per 100 ml. of blood, and at operation a tumour mass was found in the pelvis.

The duration in months from the approximate commencement of symptoms until death varied from one month to eleven months, with five cases falling in the range three to six months. Irradiation was given to one child, but this was stopped after the first dose.

Six children had a raised temperature on admission to hospital varying from 99·6° F. to 104° F. Three showed a normal temperature on admission, which later rose to 100° F. as the disease progressed.

Calcification was detected by plain X-ray examination of the abdomen in one tumour of the right adrenal gland.

Pathological Findings.

Sites of the Primary Tumours.

Six tumours were situated in the adrenal gland, with four on the right side and one on the left; one tumour was bilateral. The remaining three tumours were mediastinal, pelvic and retroperitoneal in position.

Macroscopic Description of the Primary Adrenal Tumours.

The six primary adrenal tumours could be divided on anatomical grounds into two distinct groups.

The first group, which comprised five tumours, showed a fairly uniform macroscopic appearance. They were roughly spherical in shape, and varied from 5 to 18 cm. in diameter. They were situated at the upper pole of the kidney in the anatomical site of the adrenal gland. They were, all encapsulated; the capsule varied in thickness from 1 to 5 mm., and was composed of layers of compressed areolar tissue. The underlying kidney in all cases was not macroscopically involved, but was compressed and in one instance atrophied. In one tumour the capsule had been invaded, and direct spread into the liver had occurred. The cut surface showed the tumours to be composed of nodules of irregular size separated by thin fibrous bands. Hæmorrhage was present in all, and in the bilateral example it comprised the bulk of the tumours. Areas of necrosis were prominent. Tumour tissue varied in colour from white to yellow, and in the majority was soft in consistency.

The second group comprised one tumour. This was distinct macroscopically from the others. It was a white, firm, non-encapsulated nodule 1 cm. in diameter, embedded in the substance of the adrenal gland. No areas of hæmorrhage or necrosis were seen.

The macroscopic appearance of the extra-adrenal neuroblastomata was similar to that found in the adrenal primary tumours, but necrosis was more marked.

The Pattern of Metastases.

All six adrenal neuroblastomata showed metastases to the cranial bones. The flat bones of the skull were most affected. Orbital metastases were present in two cases, and pituitary fossa secondary tumours in two. Other bones affected were the ribs and ileum. Hepatic metastases were present in five cases. The liver was moderately enlarged, and the secondary tumours appeared as yellowish-white nodules varying from 5 mm. to 5 cm. in diameter. Lymphatic spread occurred in all tumours. Mediastinal and para-aortic lymph nodes were frequently involved and cervical lymph nodes occasionally involved. Lung metastases were present in only one tumour (described above in the second group of primary adrenal tumours). These were small, white, hard nodules situated beneath the pleura. Other organs occasionally involved were the pancreas, ovary and wall of the intestine.

All three extra-adrenal neuroblastomata showed metastases to the lungs. In regard to other sites of metastases, no constant pattern was observed.

Histology.

The nine primary tumours showed various stages of differentiation towards mature sympathetic ganglion cells. For convenience they could be divided into three groups.

1. Undifferentiated — one tumour. This tumour was composed of cells varying from 10 to 15 μ in diameter, with a darkly-staining nucleus and scanty cytoplasm. The nuclei contained two or more nucleoli, and mitoses were frequent. The cells showed no structural differentiation. There was little stroma present, and necrosis and hæmorrhage were prominent. The appearance resembled a lymphosarcoma or other small round cell sarcoma (Figure I).

2. Differentiating — seven tumours. This group possessed the features outlined above in some parts, but in others the cells were arranged in small clumps of from four to twelve cells. The cell described in the first group was still present, but other cells with less darkly-staining nucleus and more cytoplasm were found. The cytoplasm of some cells was elongated into fibrillary processes. The classical rosette was found in this group; this comprised a group of cells arranged circularly about a central space. In many cases this circular arrangement was imperfect, and oval or irregularly shaped rosettes were found. In some examples fine fibrillary extensions of the cell cytoplasm were seen in the central area of the rosette. No mature nerve fibres were seen in this group. As in the first group, hæmorrhage and necrosis were prominent (Figure II).

3. Differentiated — one tumour. In this tumour ganglion cells were present in addition to the type of cell described above; nerve fibres were numerous (Figure III).

Histology of Metastases.

The histological features, as seen in the primary tumours, were not usually found in the secondary deposits. The appearance was more sarcomatous in the majority of cases. Secondary deposits in the liver showed little evidence of differentiation, and their origin was difficult to ascertain (Figure IV).

Discussion.

Neuroblastomata occur with sufficient frequency in childhood to warrant more than passing interest by pædiatricians.

The sex incidence in this series showed a predominance of males over females; however, in larger published series the sex incidence was about equal.

The disease is one of early childhood, and most cases occur in the second year of life. Neuroblastomata occur

with lessened frequency up to adolescence, and occasional cases have been described in adults.

The prominent clinical features in this series were anæmia and abdominal enlargement.

Severe anæmia was the outstanding feature on admission to hospital of four patients. Because of its frequent occurrence in childhood, acute leukæmia was provisionally diagnosed in all cases in which the hæmoglobin value was very low. In two cases this diagnosis was erroneously confirmed by marrow examination, because of the failure to recognize tumour fragments. Confusion should not occur if the following facts are remembered. Tumour cells are usually arranged in syncytia or irregularly shaped clumps. The nucleus of the neuroblastoma cell is more condensed and its cytoplasm more ragged than the blast cell. Areas of normal marrow tissue may be seen together with tumour fragments.

The diagnosis of the cause of the abdominal enlargement in these cases can be difficult. Plain X-ray examination of the abdomen may show flecks of calcification in a neuroblastoma. In this series, only one primary adrenal tumour showed calcification. The other symptom consistently present was pyrexia. Bone and joint pains were prominent and occurred frequently.

However, none of the above-mentioned clinical features is diagnostic alone. A combination of anæmia, abdominal enlargement, pyrexia and bone pain is suggestive of neuroblastoma in children under four years of age.

The site of the primary tumour in neuroblastoma is commonly the adrenal gland. The distribution between right and left sides is approximately equal in a large series of cases.

Neuroblastomata may occur wherever there is sympathetic nervous tissue, so that the distribution covers the thoracic, abdominal and pelvic regions. No cases have been described in the central nervous system.

Macroscopically, the primary tumour has a distinctive appearance, but in some cases this is obscured by hæmorrhage and necrosis.

Bilateral adrenal tumours were present in one infant, aged two days; each tumour measured five centimetres in diameter, and had the same macroscopic and microscopic appearance. From their size alone it was evident that these tumours arose before birth. Wells, in 1936, described a similar congenital origin for some neuroblastomata. Because of the early appearance in life of neuroblastoma, it is probable that some of the tumours in this series arose during fœtal development.

One feature that emerged from a study of the metastatic spread was the invalidity of the Hutchison and Pepper syndromes in this age group. It would appear that the spread of neuroblastoma followed no particular pattern, and was independent of the site of the primary tumour. Pulmonary metastases were rare in primary adrenal neuroblastoma. This fact is hard to reconcile with the theory of blood-borne metastasis. Perhaps the neuroblastoma cells can pass through the pulmonary capillaries, as suggested by Blacklock (1936). Willis (1952) contends that careful search will reveal lung secondary tumours in all cases. This has not been our experience.

The terminology employed for this type of tumour has varied from sympathoblastoma to neurocytoma. The term neuroblastoma has come to be generally applied. Some objection has been raised to this term on the grounds that differentiation of the tumour cells may proceed to chromaffin cells. However, this occurs infrequently and does not justify changing the name on that account.

During fœtal development, the first cells recognized in the developing sympathetic system are called sympathogonia. These are cells with a darkly-staining nucleus and scanty cytoplasm; cells called sympathoblasts with a vesicular nucleus and more cytoplasm are a further stage in development, leading progressively to mature sympathetic ganglion cells. On this basis Blacklock, in 1936, divided neuroblastomata into groups according to the type of cell present.

Although an embryological classification has apparent merit in that it divides neuroblastomata into sub-groups, the grouping has little practical value. Also, the identification of many of the developing cells is difficult. The embryological subdivision are arbitary and lose sight of the concept of progressive differentiation towards maturity, with cells of an intermediate nature being present in most tumours.

Microphotographs of rosettes are conspicuous in textbooks of pathology describing the neuroblastoma; however, because of the relative infrequency of rosettes seen in this series, it would appear that the rosette has been over-emphasized. A more outstanding characteristic was the presence of clumps of cells — the so-called "markballen". These clumps are readily seen in developing sympathetic tissue, and can be found in the adrenals of neonates and young children up to the age of ten years.

The nature of the fibrillary material inside the rosette is generally claimed to be neural. Attempts at staining these fibres by the Bielschowsky technique gave variable results, and was of little aid in routine diagnosis.

One tumour showed ganglion cells, together with frank neuroblastomatous elements. This finding raised the question of malignant disease supervening in a mature ganglioneuroma. This view is denied by Willis (1952), who states that since mature ganglion cells do not divide, a malignant transformation is impossible. The presence of the ganglion cells is better explained by the progressive maturation of the neuroblastoma cell, and is only one facet of the tumour.

The sarcomatous appearance of the metastases in the liver presents obvious diagnostic difficulties. The typical appearance, as seen in the adrenal, is frequently absent, and a correct diagnosis can be reached only by a consideration of both the clinical features and the cytology.

Summary.

The clinical details and autopsy findings in nine cases of children who died of neuroblastoma are reviewed. Either severe anæmia or abdominal enlargement was the outstanding finding on admission to hospital.

In those cases with low hæmoglobin values, tumour deposits in the bone marrow should not be confused with acute leukæmia.

No basis in fact is found for the Hutchison and Pepper syndromes. The progressive degree of differentiation in neuroblastoma is emphasized, and the difficulties in pathological diagnosis are stressed.

Acknowledgements.

I wish to thank Dr. J. Perry and Dr. A Williams, of the Pathology Department of the Royal Children's Hospital, for their advice. I am also indebted to the medical staff of the Hospital for access to the case records.

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Legends to Illustrations.

FIGURE I.—Undifferentiated neuroblastoma resembling a sarcoma. (× 350.)

FIGURE II.—Differentiating neuroblastoma. The cells are arranged mainly in clumps, but a rosette can be seen in the centre of the field. (× 350.)

FIGURE III.—Differentiated neuroblastoma. Imperfect ganglion cells and nerve fibres are present. (× 350.)

FIGURE IV.—Metastasis in liver showing little evidence of differentiation. (× 350.)

Reports of Cases.

CONSTRICTIVE PERICARDITIS FOLLOWING HÆMOPERICARDIUM FROM MILD NON-PENETRATING TRAUMA TO THE CHEST.

By WILLIAM S. ROWE, M.R.A.C.P.,
Brisbane.

IT is the purpose of this report to draw attention to a sequence of events hitherto uncommon, but likely in the future to be seen considerably more often.

Clinical Record.

A male patient, a timber cutter, six feet tall, 15 stone in weight and well muscled, was admitted to the Brisbane Hospital on August 22, 1956, with a letter from his country doctor, stating that he had been well until some three weeks before, when he had begun to lose his normal effort capacity and to develop flatulent dyspepsia and exertional dyspnœa. One week later the patient had noted the presence of ankle œdema, and had found it necessary to sleep propped up. For the week preceding his reference to the Brisbane Hospital he had been in bed in the local hospital receiving digitalis and mersalyl, despite which his general condition had continued to deteriorate. He had been anorexic for some days, and for the last three days his sputum had been blood-stained. He had had no fever or chest pain at any stage. The patient's history confirmed this account. Over the previous three weeks he had found it necessary to quit his usual occupation (using a chain-saw weighing 40 pounds) for lighter work, and finally to abandon work altogether. There was no significant past history of illness, and his general health had always been excellent.

On examination, on the night of his admission to hospital, the patient was found to be hyperpnœic though propped up in bed. His face was somewhat suffused. The jugular venous pressure was greatly increased, and veins on his forehead were engorged. The apex beat was impalpable, but the area of cardiac dulness was much increased. His heart sounds were rather faint, and every other first heart sound at the apex was louder—that is, ventricular pulsus alternans could be heard. The pulse rate was 132 per minute and regular, but the pulse was not regular in amplitude, in that it tended to become impalpable during inspiration. Auscultation over the brachial artery confirmed the presence of pulsus paradoxus from 130 to 110 millimetres of mercury. The blood pressure was 130/80 mm. of mercury. There were marked ankle œdema and some sacral œdema. Good air entry was heard in both lungs, with a few crepitations at both bases. The patient's abdomen was distended and tympanitic; no shifting dulness was present. The liver was tender and enlarged to below the level of the umbilicus.

A provisional diagnosis of pericardial effusion with early cardiac tamponade was made. Immediate fluoroscopic examination revealed a very large cardiac shadow and some pulmonary congestion, but no pleural effusion. Cardiac movement was almost completely absent (Figure I). An electrocardiogram showed marked electrical pulsus alternans, decreased voltage and flat or inverted *T* waves in all leads—all suggestive of a pericardial effusion with some degree of tamponade (Figure IV).

An initial period of expectant treatment was considered reasonable, and during the next two days the patient's symptoms and signs remained much the same, and a second fluoroscopic examination on August 24 revealed no change. The same day he passed 62 ounces of urine after an intramuscular injection of mersalyl. His erythrocyte sedimentation rate (measured by the Wintrobe method) was 4 mm. in one hour, the hæmoglobin value was 12·2 grammes per 100 ml., the leucocytes numbered 17,000 per cubic millimetre (neutrophils 90%), and the microscopic findings in the urine were within normal limits. He had now developed a low-grade fever.

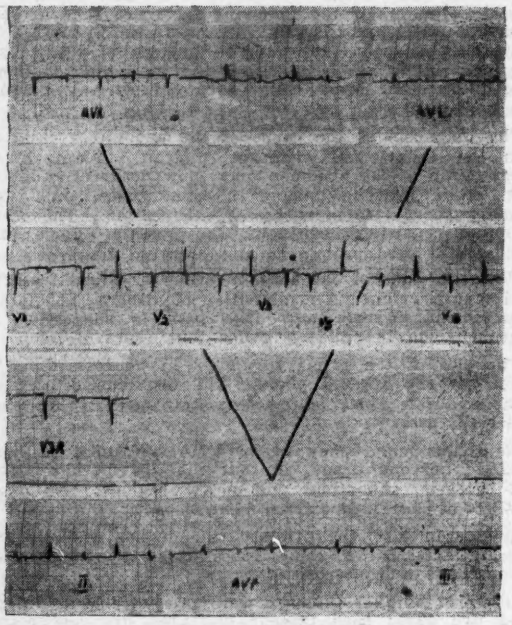

FIGURE IV.
Electrocardiogram taken before the pericardial tapping, showing electrical pulsus alternans.

On August 25 (three days after his admission to hospital) his general condition appeared to be deteriorating, so a pericardial paracentesis was performed through the fifth left intercostal space just outside the nipple line. The exploring needle had not been inserted very far when aspiration produced thin black fluid, which did not clot on standing, and which had the appearance of old blood. (This fluid was, in fact, first encountered with the short needle used to anæsthetize the track for the aspirating needle.) Six hundred and sixty millilitres (22 ounces) of this fluid had been aspirated, with gradual advancement of the needle, when the latter was felt momentarily to touch the heart, whereupon the procedure was promptly discontinued.

On examination of the patient immediately after the aspiration, pulsus paradoxus could no longer be felt at the wrist (although it was present still on auscultation from 130 to 120 millimetres of mercury), and the ventricular pulsus alternans had disappeared. The heart sounds were louder, and a pericardial friction rub was faintly audible. The apex beat was definitely palpable in the mid-clavicular line in the fifth left intercostal space. The forehead veins were no longer distended.

Fluoroscopic examination now revealed definite cardiac movement, and a double shadow was visible consisting of an inner, denser shadow whose border displayed most movement, and an enveloping, less opaque shadow, the whole being a little smaller than before aspiration (Figure II). An electrocardiogram two hours after aspiration showed disappearance of the electrical pulsus alternans, more definite upright *T* waves and no fresh abnormalities (Figure V).

From then on his condition steadily improved, except for an episode of chest infection complicating some atelectasis of the lower lobe of the left lung, and accompanied by a small pleural effusion and a fever which subsided quickly on antibiotics. Mersalyl given on the second and fourth days after the pericardial tapping produced 160 ounces and 140 ounces respectively of urine, and the patient became œdema-free within a few days. His heart rate slowed to 80-90 per minute, and he developed a moderately loud pericardial rub maximal a little medial to the apex beat. One week after the tapping his liver size was reduced to three fingers' breadth below the right costal

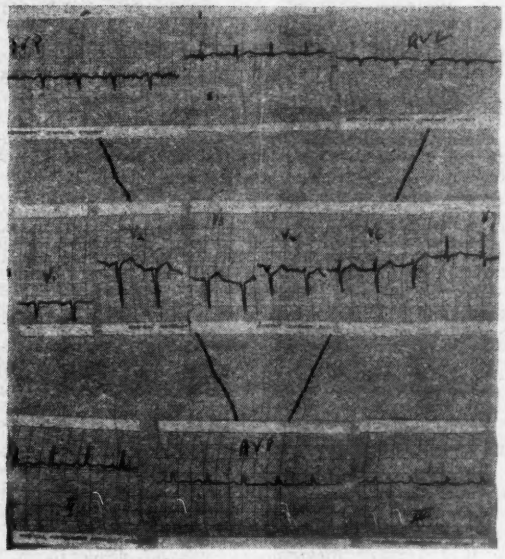

FIGURE V.

Electrocardiogram taken after the pericardial tapping, showing disappearance of the electrical pulsus alternans.

margin, his abdomen had lost most of its tympanitic distension, and he no longer complained of flatulence. The platelet count, clot retraction, and bleeding, coagulation and prothrombin times were all within normal limits; examination of the fæces revealed no occult blood, and Mantoux tests (with old tuberculin 1:1000 and 1:100) gave negative results.

Further questioning of the patient at this stage elicited the fact that some two weeks before the onset of symptoms —that is, some five weeks before his admission to the Brisbane Hospital—he had fallen forwards, striking the left upper quadrant of his chest quite a sharp blow on the (pointed) handle of his axe. Beyond being momentarily "winded", he had experienced no immediate ill effects, and had not considered the incident significant enough to warrant mention. The blow did not bruise his chest.

The patient was confined to bed for a considerable period, and then slowly mobilized. His general condition throughout this period was good except for the presence of a persistent left pleural effusion, which was aspirated on October 23, and which consisted of brownish-red, thin fluid with the appearance of an old blood-stained pleural effusion. At the time of his discharge from hospital on December 20, 1956, there was no ankle œdema or hepatomegaly, and the jugular venous pressure was normal. His heart had also gradually returned to normal size (Figure III).

Over the ensuing months, despite digitalis and mersalyl therapy given by his local doctor, he began to develop ankle œdema again, and his liver again became palpable. By August, 1957, it had become apparent that he was developing the constrictive syndrome, and pulsus paradoxus, which had never entirely disappeared, was once again present over a wide range. The patient at this stage volunteered the observation that he "couldn't feel his heart beating in his chest any more" when he walked up a hill.

On January 22, 1958, he was readmitted to hospital for preparation for pericardiectomy; but all measures, incuding the administration of cation exchange resins, "Chlorothiazide" and other diuretics (as well as repeated aspiration of the abdomen and thorax) failed to relieve

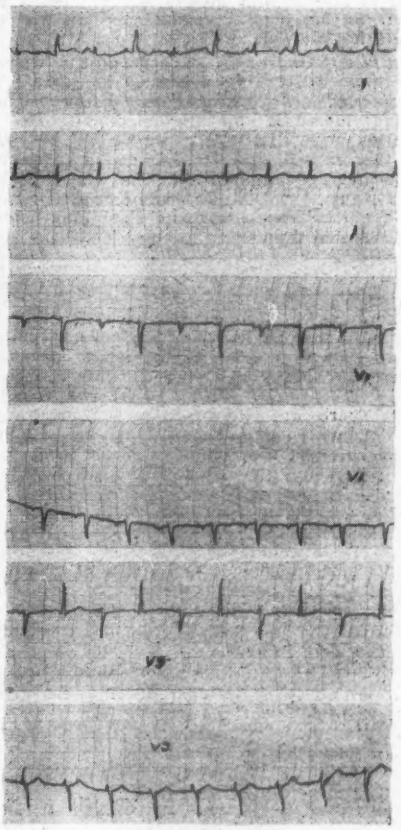

FIGURE VI.

A selection of leads from electrocardiograms before and after the pericardial tapping, arranged for purposes of comparison.

the œdema, ascites, gross hepatomegaly and right hydrothorax which had by now developed. The serum bilirubin level at this time was 3 mg. per 100 ml., the serum alkaline phosphatase content was 8·9 King-Armstrong units, and flocculation tests and serum electrophoresis gave normal findings, with a total serum protein content of 7·8 grammes per 100 ml.

On May 1, 1958, the pericardium was explored by Dr. Morgan Windsor, through a transverse incision dividing the sternum at the fifth intercostal space. The heart and the bases of the great vessels were found to be wholly encased by a tight, fibrotic envelope 3 mm. thick. There was minimal pulsation at the apex and no pulsation over the right ventricle or right atrium. The extrapericardial tissues were normal. The "peel" was smooth, its internal lining closely constricting all chambers, and attached by fine areolar strands to the myocardium. There was no evidence of myocardial trauma. Pericardiectomy was performed from phrenic nerve to phrenic nerve and from the base of the great vessels to the diaphragm. The posterior surface of the heart was not decorticated.

Finally, the right pleural sac was opened and the hydrothorax aspirated. Dr. J. J. Sullivan reported that microscopic examination showed the removed pericardium to consist of "dense virtually acellular fibrous tissue with abundant iron pigment present". There was no evidence of any underlying infective process (Figure VII).

The post-operative period was uneventful, and the patient was discharged from hospital on June 6, 1958, taking digitalis and "Chlorothiazide". At the time of his discharge he had very slight œdema, his liver had decreased in size to four fingers' breadth below the right costal margin, his jugular venous pressure was +4 centimetres and he felt well.

He was last examined on August 14, 1958, when he was well. He was still taking digitalis and mersalyl once a week, but did not think that his urinary volume was appreciably increased by the mersalyl. He had no exertional dyspnœa. There was slight ankle œdema, though he said that it was steadily decreasing in degree. The jugular venous pressure was not raised, and his liver was barely palpable. An X-ray examination of his chest revealed a normal-sized heart and clear lung fields, except for some residual thickening at the base of the right lung.

Discussion.

An extensive search of the literature does not reveal many references to the occurrence of hæmopericardium following mild trauma to the chest with a blunt instrument. There are even fewer reports of the development of constritive pericarditis as a sequel of hæmopericardium so produced—and very few of these patients have had a happy outcome. There are, however, a sufficient number of reported instances of constrictive pericarditis following hæmopericardium (from blunt or penetrating injury) as to leave little doubt that organization of clotted blood on the pericardium can ultimately result in constriction (Ada *et alii*, 1950; Deterling *et alii*, 1955; Ehrenhaft *et alii*, 1952; Elkin *et alii*, 1951; McKuisick *et alii*, 1955; Overholt *et alii*, 1952). It would appear that whether or not fresh clot or only old liquid blood is found in the pericardial sac depends on the time interval between the injury and pericardiotomy (Elkin *et alii*, 1951; Seror *et alii*, 1957). Experimentally, it has been shown that constrictive pericarditis can be produced in dogs by intrapericardial injections of blood (Ehrenhaft *et alii*, 1952).

Pericardiotomy with evacuation of blood and clot at the time of the pericardial tapping might possibly have prevented the later development of constriction, although in a case of hæmopericardium following chest trauma with a blunt instrument "considerable organization overlying the epicardium of the entire heart" was found at autopsy eleven days after the trauma, and it was considered from the appearances that "constrictive pericarditis would almost certainly have developed had the patient lived" (McKuisick *et alii*, 1955). Similarly, Skinner and Farr (1953) reported the case of a patient who was treated initially by pericardial tappings for acute hæmopericardium from a knife wound, and in whom operation five weeks later revealed organized blood clot already constricting the right side of the heart. The "peel" separated easily, with immediate increase in right auricular filling and stroke volume, and the patient made an uneventful recovery.

The occurrence of electrical pulsus alternans is in accord with the findings of McGregor and Baskind (1954) and others (Mincuzzi *et alii*, 1957; Piso, 1956), and supports the view that it may be a useful confirmatory sign of the presence in the pericardial sac of a significant amount of fluid. McGregor and Baskind, in a review of 58 cases of proven pericardial effusion, also stated that "in the only three cases in which observations were made immediately before and after paracentesis, this procedure resulted in cessation of the electrical alternans". In another of their cases alternation of intensity of the heart sounds was noted. The findings in our case again conform with their observations.

In view of the ever-increasing frequency of automobile accidents, many of which involve "steering wheel injuries" to the chest, it seems reasonable to assume that the incidence of constrictive pericarditis occurring as a result of "blunt" trauma to the chest will also steadily increase —notwithstanding the fact that some monographs on cardiology do not yet mention this cause in their discussion of the ætiology of constrictive pericarditis.

Summary.

A case is reported of a patient with constrictive pericarditis, which occurred as a sequel to hæmopericardium following mild trauma to the chest with a blunt instrument, and which has been successfully treated by pericardiectomy. It is believed to be the first such case to be reported in the Australian literature.

The significance of the accompanying electrocardiographic changes is discussed.

It seems likely that an increasing number of cases of constrictive pericarditis from this cause will be seen in the future.

Acknowledgement.

I should like to thank Dr. A. D. D. Pye, General Superintendent of the Brisbane Hospital, for access to hospital records and X-ray films.

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Addendum.

The patient was last seen on May 28, 1959, when he appeared very fit and had no œdema or hepatomegaly. He said that he had recently been mustering and dipping cattle on a relative's property, and also helping to clear scrub there, with excellent exercise tolerance and no undue exertional dyspnœa.

Legends to Illustrations.

FIGURE I.—Skiagram taken on the night of the patient's admission to hospital (August 22, 1956).

FIGURE II.—Skiagram taken on August 25, after the pericardial tapping, showing the double shadow.

FIGURE III.—Skiagram taken on December 12, 1956.

FIGURE VII.—Photomicrograph of the pericardial "peel". Prussian blue stain, showing dense fibrous tissue containing clumps of iron pigment. (×160.)

CONGENITAL HÆMANGIECTATIC HYPERTROPHY WITH MELÆNA AND CHILDBIRTH.

By G. S. SANTOW,
Sydney.

EARLY in 1954, I had the opportunity of examining a patient presenting most unusual vascular anomalies. She was an unmarried woman, aged 23 years, employed as a pathology technician in a research laboratory. In the course of a routine examination of the personnel of the laboratory, she was found to have hypochromic microcytic

anæmia of the iron-deficiency type. After this discovery she was sent to see Dr. T. Orban, who referred her to me.

The patient gave the following history. She was alleged to have been a "blue baby" at birth, simply because of a peculiar purple discoloration of the lower half of her body from the hips down. (This discoloration is still present.) At the age of five years, after a day on the beach, she had an attack of severe pain over the left leg. The skin over the whole of the calf and the foot was painful to touch; movements were painful only because of tension over bending joints. No abnormality was visible over the area, and the mother denied that sunburn might have been the cause. This first attack of pain and swelling lasted for two or three days, and over the next 12 months the patient had several attacks lasting for minutes only. The left ankle was larger in circumference than the right, and both legs were larger, heavier and thicker than normal. Rest in bed brought about a reduction in the size of the swellings, but after half an hour's walking the limbs swelled again. Puberty was normal; the menarche occurred at the age of 11 years, with rather excessive menstrual losses at first. The menstrual periods were regular. At the age of 18 years the patient had an attack of "appendicitis"; but at operation a large ovarian cyst was found, the presence of which explained the clinical symptoms. The appendix was large, but not inflamed. Appendicectomy with partial oophorectomy was carried out by Dr. A. E. Moir at St. Luke's Hospital. The large size of the pelvic vessels was noted at the time of the operation. Whilst she was convalescing from the operation, the patient contracted pleurisy in hospital.

A few months after the operation, a routine investigation showed that the patient's hæmoglobin value was 10·5 grammes per 100 ml. This check was needed, as she was working with radioactive material. Approximately nine months after the operation, the patient began to have attacks of melæna before almost every menstrual period. (From the time of the operation the periods have been painful; she suffers from dysmenorrhœa for two days.) The hæmoglobin value did not improve, though she gave up her work with radioactive materials.

In November, 1951, the patient received her first blood transfusion. After she had received three bottles, she had a severe headache and a stiff arm for three months. One month after the transfusion she had a "sort of heart attack"; however, an electrocardiogram showed no abnormalities. At this time she was receiving injections of liver and vitamin B_{12}, and also iron by mouth. Serious stomach upsets caused her to cease taking iron. Attacks of melæna became more severe, and her menstrual periods were no longer regular.

In June, 1952, she received a second blood transfusion; a reaction occurred after she had been given one bottle, with headache, backache, shivering and rigors with fever, and she felt very ill. She was unconscious for two days. Pain was present in all her muscles. She had no difficulty in passing urine, which was normal. This last transfusion was given because the hæmoglobin value had fallen to six grammes per 100 ml. One week after the transfusion the hæmoglobin value was 7·9 grammes per 100 ml. She was transferred from St. Luke's Hospital to Sydney Hospital under the care of Dr. A. J. H. Stobo, with the diagnosis of simple blood loss anæmia. At a previous consultation a surgeon had refused to operate on her for hæmorrhoids, because of the large vessels in the rectum and also because of her poor general condition. While she was in Sydney Hospital, two weeks after another blood transfusion, the hæmoglobin value was found to be 7·5 grammes per 100 ml. The patient was prepared for hæmorrhoidectomy; however, the anæsthetist refused to take the risk.

At home the patient was again given vitamin B_{12} and liver by injection and iron by mouth. However, she continued to suffer from diarrhœa and fairly copious blood loss *per rectum*. By this time she had for three months been taking "Ferronicum", had been suffering intermittently from abdominal pain and had had severe attacks of rectal hæmorrhage. At the last estimation of the hæmoglobin value it was found to be 5·9 grammes per 100 ml., and the patient was mostly in bed. There was some mucus in the stools. The menstrual periods were no longer heavy — if anything, they were rather slight. She had several teeth extracted without undue blood loss. There was no bruising and no tendency to bleed from the upper half of the body; bruising occurred easily only on the legs. She was now exhausted by walking even short distances.

It was at this time (July 23, 1954) that I made the acquaintance of the patient. She was spending most of the day in bed because of her feeling of exhaustion, and also because her medical attendant was trying to build up her strength and increase her hæmoglobin value in preparation for hæmorrhoidectomy. At this time, on both the patient's legs and thighs, over the buttocks and in front up to the level of the navel, there were areas of strawberry-coloured skin (Figure I). The areas were

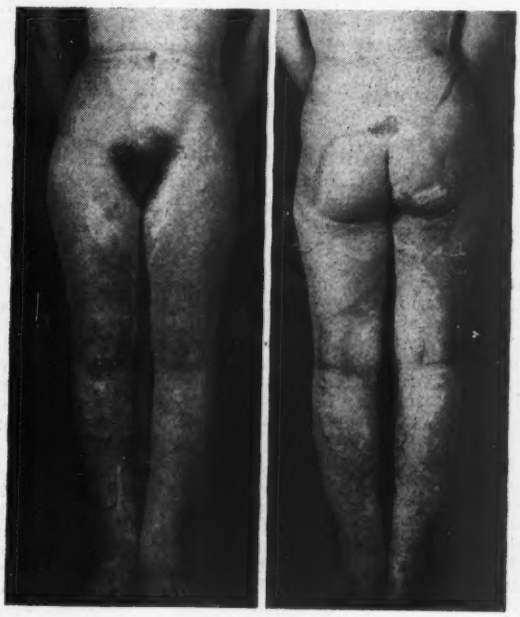

FIGURE I.

not raised, and they covered most of the lower limbs and part of the lower part of the abdomen, the mid-line being left free. This area showed the fine vascular design commonly found in hæmangiomata or flat nævi of the skin, the deep red hue disappearing upon pressure with a cover-glass. In both feet, legs and thighs, both groins and both labia there were distended veins. The veins were not distributed according to the regular course of saphenous varicosities as observed in varicose veins of the lower extremities. No regular pattern of venous distension was discernible in the field of the greater or lesser saphenous vein and their usual tributaries. The dilated veins formed a network of no set design, reaching up to the level of both hips. Both legs were heavier and thicker than the patient's height and build would suggest. The normal contours of the feet and ankles were obscured by the spongy swelling caused by venous engorgement. This appearance of swelling was more pronounced on the left side than on the right. On elevation of the legs with the patient supine, their size decreased, the engorgement and swelling receded and the deep red hue became paler. This process was reversed by the patient's standing erect. The so-called Trendelen-

burg phenomenon was not elicited, as the legs filled with blood through the deep venous channels above and below the foramen ovale on both sides. The condition of the legs described, as well as that of the whole body from the waist down, had been noticed by the mother at the patient's birth.

At this time, as operation was contemplated, X-ray films of the patient's skeleton were taken; these showed no abnormality. The skiagram of the pelvis is reproduced in Figure II. This calls for some comment. In the common iliac veins of the pelvis, large phleboliths were shown; they were so large and so extensive in a young woman of the patient's age that they could not be passed over as of no interest or significance. Since there was in this patient extensive maldevelopment of the vascular system, visible to the naked eye, it was obvious that the X-ray appearance of the common iliac veins should be carefully noted.

Investigation of the blood chemistry gave normal values. A rectosigmoidoscopic examination was carried out, as it was necessary to ascertain whether a somewhat extended Whitehead operation would be sufficient to deal with the melæna. The findings were as follows. The sigmoidoscope was inserted to a distance of 21 centimetres. Dilated and bleeding vessels were seen in the lower ampulla, from the anal margin extending upwards to involve the external and internal hæmorrhoid plexuses. Instead of discrete nodes, the appearance was that of diffuse, dilated, richly anastomosed venous plexuses. Beyond the internal sphincter muscle, the mucosa of the rectum was essentially normal.

Operation was undertaken on July 26, 1954. A circular resection of the rectal mucosa up to and including the internal hæmorrhoid plexus was carried out; the sphincter ani was carefully preserved, and a small strip of rectal mucosa was left anteriorly and posteriorly to prevent stricture formation. All veins were carefully ligated, and blood loss was not excessive. A blood transfusion of two pints was given after operation without reaction. The patient left hospital on August 6. However, two days later she developed pain in the chest and a rise of temperature, and was readmitted to hospital with pulmonary infarction. She was discharged, well, three weeks later.

Two years after the operation, the patient came to inform me that she had been in perfect health for two years, that her anæmia had disappeared, and that she was now married. The modification of her social status triggered off a series of problems. On examination, she was found to be two months pregnant. Elsewhere she had been advised to seek interruption of the pregnancy because of the vascular abnormalities described above. Subsequent events proved that that advice was unnecessary, since she was successfully steered through the pregnancy.

At the beginning of pregnancy the patient weighed eight stone, and her blood pressure was 120/65 mm. of mercury. Her blood group was A, Rh-positive. From the twelfth week of gestation, the size of the patient's legs did not alter after the night's rest. From that time the labia began to enlarge grossly, because of the varicose veins in them. At 24 weeks the blood pressure was 135/85 mm. of mercury, and a salt-free régime was instituted. By this time the labia had enlarged to the size of small aprons, and the circumference of both lower limbs had increased considerably owing to venous congestion. During pregnancy there was no rectal bleeding. The expected date of confinement was calculated as March 10, 1957. However, by February 19 the blood pressure rose to 140/90 mm. of mercury, and the patient was therefore confined to bed in hospital. Even with appropriate diet, and the exhibition of rauwolfia and sedatives, the blood pressure gradually rose to 160/95 mm. of mercury, and a trace of albumin appeared in the urine. The fœtus was in the left occipito-anterior position, and the presenting part showed no tendency to engage. Because of the presence of pre-eclamptic toxæmia in association with a non-engaged head, it was thought that disproportion might have to be dealt with. An X-ray examination carried out by Dr. A. Owen revealed the following diameters: conjugata vera 9·8 cm., antero-posterior mid-plane 9·8 cm., available outlet 9·5 cm. The inlet was platipeloid. Even with a fœtal head of average size, these gave uncertain prospects for vaginal delivery. Lower segment Cæsarean section was performed without trial labour, the patient having had adequate treatment for toxæmia in hospital without any tendency towards improvement. A normal female child was delivered, who cried immediately, and showed none of the vascular abnormalities of her mother. During the operation, it was noted that extraordinarily large venous sinuses were present in the lower uterine segment.

Comment.

It now remains to discuss the nature of the vascular abnormalities found in this case and their possible bearing on clinical problems.

Parkes Weber (1949) describes the clinical picture of hæmangiectatic or telangiectatic hypertrophy of limbs; this disease is often named after him. However, a similar condition described by French authors is called the syndrome of Klippel-Trénaunay. This, of course, is a further argument against giving syndromes the names of authors. In this sense the condition is well defined in the title of this report. Parkes-Weber draws attention to the possibility of arterio-venous shunts, but this can be excluded.

The congenital type of hæmangiectatic hypertrophy has been known to occur in the upper limbs, more often in one arm than in both. Petit and Braun-Tapie collected 12 cases of congenital varicose veins of the lower extremities, all associated with capillary angiomata. In many cases hypertrophy of the skeleton, symmetrical or only in one limb, has been reported. In the case recorded in this paper there were no bony changes and no asymmetry in the growth of the shafts of the long bones. The hæmangiomatous state in embryonic and post-embryonic life may contribute to the growth of bones by providing abnormally increased blood supply and nutrition. The term congenital varicose veins should not be used for such cases as the present. Varicosities in veins are essentially due to pathological changes in the walls of vessels leading to incompetence of the valves; this in turn leads to further widening of the calibre of veins through stasis, etc. Telangiectatic nævi spread asymmetrically over large areas of the body are associated with telangiectatic veins. Both have the same cause — error in development (dysgenesis). They should not be called congenital varicose veins, except, perhaps, to describe their superficial likeness to something which they definitely are not. The difference between telangiectatic "congenital veins" and the veins in nævi is only one of size, and not one of quality. They have identical origins.

In this paper hæmangiectatic hypertrophy has been discussed as a congenital malformation. From clinical observation of this patient, I have come to the conclusion that any necessary surgical treatment can be undertaken in similar cases if the customary indications for such treatment are present. Hæmangiectatic hypertrophy seems to spread only into parts which are clearly marked with the "red light" of nævi—one or two limbs, the rectum, the veins of the pelvis. One appreciates the fact that the condition is not a truly systematic congenital malformation—one that affects the whole of the mesenchyme, for instance — but a malformation affecting only a limited section. Confidence in dealing with any clinical problems presenting in such cases should be restored by the foregoing observations.

Summary.

A case of congenital hæmangiectatic hypertrophy is presented, and some of the problems associated with the condition are discussed.

Acknowledgement.

My thanks are due to Dr. T. Orban, pathologist, for his help in carrying out all the necessary tests and investigations.

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TWO CASES OF EPIPHRENIC DIVERTICULA OF THE ŒSOPHAGUS.

By GORDON CHAMBERS, M.B., B.S.,
Late Resident Medical Officer, Royal Adelaide Hospital, Adelaide.

UNTIL 1952 only 123 cases of epiphrenic diverticula had been reported in the literature (Goodman and Parnes, 1952).

The first case presented here is of interest because (i) distension of the diverticulum was associated with attacks of asthma; (ii) the prolonged administration of cortisone might have had some ætiological bearing on the condition. The second case was discovered incidentally during investigation of a thyroid carcinoma, and was virtually asymptomatic.

CASE I.—Mrs. A., aged 57 years, had been admitted to the Royal Adelaide Hospital 16 years previously suffering from severe asthma. After discharge from hospital she had suffered attacks almost nightly until she was readmitted in status asthmaticus 13 years later. Cortisone therapy was commenced, and thereafter asthmatic attacks were almost abolished and the patient was discharged.

Dysphagia first appeared 16 months before death, and was alike for solids and liquids. Food would "stick" in the lower part of the œsophagus with associated regurgitation and lower substernal burning pain. An œsophagoscopy performed at this time was followed by several weeks' freedom from dysphagia, though no abnormality had been recorded. Anticholinergic drug therapy provided relief for several months, but dysphagia returned.

On her readmission to hospital in September, 1957, an intramuscular injection of atropine, 0·01 of a grain, abolished the dysphagia for approximately four hours. A meal frequently precipitated an attack of asthma, presumably owing to the accumulation of fluid in the lower part of the œsophagus, cortisone therapy having been suspended because of a diminishing effect. If regurgitation of some of this fluid was accomplished, the bronchospasm eased, but usually either adrenaline or aminophylline given intravenously was required.

Examination showed a thin apprehensive woman with the signs of advanced emphysema.

X-ray studies revealed a diverticulum of the œsophagus 7 to 8 cm. long, involving the lower part of the middle third. The outline was regular and contractility remained (Figure I).

A second œsophagoscopy revealed no abnormality, and in fact the cardia was found to be lax. However, this might have been the result of an injection of atropine which had been given for premedication.

Because of developing resistance to cortisone, therapy had been changed to ACTH for several weeks. Asthma became worse and therapy with steroids was resumed. The patient improved, and was having less severe and less frequent asthma when a sudden severe attack developed and proved fatal within a few minutes.

At autopsy the lungs showed generalized emphysema with aspiration of gastric contents into the bronchial tree.

The adrenals were very small and flattened. In the œsophagus there was a diverticulum, 6 cm. long and 2·5 cm. wide, with the lower border 6 cm. from the gastro-œsophageal junction (Figure II). The œsophageal wall from the cardia to the junction of the middle and upper thirds was grossly hypertrophied, and measured 0·5 to 0·75 cm. thick (Figure III).

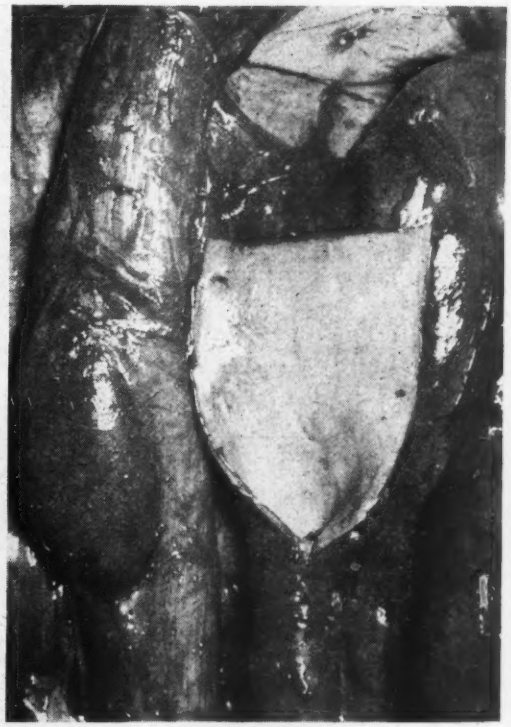

FIGURE II.
The diverticulum (Case I). The thoracic aorta is shown on the right, partly opened out.

On microscopic examination of the œsophageal wall no abnormal glandular rests were seen, and one Meissner corpuscle was found. All coats of the normal œsophagus were present in the diverticulum, although the muscle layers were very thin.

CASE II.—Mrs. B., aged 48 years, had had a partial thyroidectomy performed in Germany in 1950 for thyrotoxicosis. Five years later she discovered a hard lump in the left side of the neck, and one year later dysphagia at the level of the thyroid appeared.

The patient was admitted six weeks later (July, 1957) to the Royal Adelaide Hospital for investigation.

X-ray studies demonstrated a large diverticulum arising from the right side of the œsophagus just above the diaphragm (Figure IV). The barium readily flowed into the stomach after filling the diverticulum.

Histopathological examination of the biopsied cervical gland revealed a secondary deposit from thyroid carcinoma. A total thyroidectomy was then performed, followed by a radioactive iodine uptake test and later by radioactive iodine therapy.

In June, 1958, five months after receiving the I^{131}, the patient was apparently free from symptoms of the carcinoma. However, regurgitation of fluids occurred five minutes to an hour after some meals. This occurred only about once in three days if the patient restricted fluid intake with her meals. When regurgitation occurred it was forceful and uncontrolled. Even in reply to leading questions, she did not admit to discomfort of the lower part of the œsophagus, but stated that the trouble was at the level of the thyroid cartilage.

Comment.

The diverticulum in Case I was a true diverticulum as stated by Bockus (1943), having all muscle layers

FIGURE III.

The thick œsophageal wall (Case I). The edge of the diverticulum is slighly folded on itself. A, œsophagus; B, lung; C, hypertrophied wall; D, diverticulum; E, opened aorta; F, lung; G, liver.

in its wall. It projected from the posterior wall of the œsophagus, but was visible on the right side on radiographic examination. Most epiphrenic diverticula project from the right side of the anterior wall, according to Cornell (1956). This was so in Case II. Dessecker (1924) reported 12 cases, in which nine projected to the right, two directly posteriorly and one to the left of the œsophagus.

Epiphrenic diverticula usually do not cause symptoms until the fifth or sixth decade, and 80% occur in males (Cornell 1956). Both presented cases were in women, the first having reached the fifth decade but not the second; symptoms in the latter case were mild and disguised by the presenting condition.

The pathogenesis of the disease is obscure.

It may be thought that intermittent lower œsophageal hypertrophy and raised intraluminal pressure could well be followed by diverticulum formation. However, Johnstone (1949) argues that an obstruction of the lower end as in Case I is unlikely to be a cause, as he examined over 200 cases of achalasia without finding a single diverticulum. The variation from achalasia in this case was the absence of any constriction at the cardia seen on œsophagoscopy, the lack of relief after the second dilatation by the œsophagoscope and the extensive hypertrophy of the œsophageal muscle. Atropine gave complete temporary relief of the dysphagia.

Case II differs from the description of Johnstone (1949) in the relative lack of symptoms and the absence of demonstrable obstruction of the lower part of the œsophagus. Weakening of the wall by peptic ulceration was not definitely excluded, but freedom from epigastric pain suggested its absence.

It is not known whether the prolonged administration of steroid therapy played any part in the production of the epiphrenic diverticulum in Case I.

Acknowledgements.

I wish to thank the Medical Superintendent, Royal Adelaide Hospital, for permission to publish these cases, and Dr. K. Stuart Hetzel, under whom the patient in Case II was admitted. I am indebted to Mr. Mark Bonnin, under whose care the patient in Case I was admitted, and for his help in writing these reports.

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Legends to Illustrations.

FIGURE I.—Skiagram showing the diverticulum of the œsophagus (Case I).

FIGURE IV.—Skiagram showing a large diverticulum arising from the right side of the œsophagus just above the diaphragm (Case II).

Reviews.

Basic Surgery. Edited by Leslie Oliver, M.B., B.S., F.R.C.S., F.R.A.C.S.; 1958. London: H. K. Lewis and Company, Limited. 9½" × 6¼", pp. 1376, with 680 illustrations (including four coloured plates). Price: £6 6s. (English).

OUR undergraduates' choice of a textbook of surgery is probably determined by the prices prevailing on the second-hand market, or is based on the unreasonable conservatism of a teacher who advocates a textbook which was good enough to guide him through his final examination, but which he has never reread critically since. Whatever the reason, it is certainly true that a very few books have been singled out and have enjoyed immense popularity within the past ten years. More recently, however, we have seen several new publications to challenge the reign of the old favourites. Some have been extensive revisions of texts which have already gone through many editions; others, like this present one, are entirely new.

If one attempts to analyse the motives which lead to the publication of yet another general textbook for undergraduates, it is hard to believe that the hope of material reward does not feature somewhere, however little, for success in this field of medical publication can be assumed to mean big business. If we use the yardstick of sales value to measure "Basic Surgery" it is hard to believe that it will succeed. It is true that, as judged by bulk for the money, it does not do too badly; but the presentation is stodgy and unattractive and unlikely to please the undergraduate, who has proved by his custom that he is not ashamed to admit to a strong predilection for the photograph and the diagram rather than for the relative tedium of the written word. It may be proper to pay no heed to such unreasonable requirements; but that

can still be made no excuse for the poor reproduction of X-ray films and some very indifferent line drawings. No, we cannot see it becoming a best-seller.

But it may be that the authors have not been looking for brisk sales and for quick progression to a second edition, but have had an urge to produce something better, something to make good the deficiencies of the other textbooks available—a new method of presentation, a new line, a new emphasis. If that was their purpose they have surely succeeded, for they have set aside a full consideration of many of the basic problems of surgical practice, such as wound healing and the prevention of infection, to make room (or so at least it seems) for a very detailed consideration of the specialties. Of the text, 15% is devoted to thoracic surgery and only a little less to neurosurgery. Our complaint is not that these are badly done; quite the reverse is true. The chapters on lung abscess and bronchial carcinoma are excellent, and that on surgical considerations of cranial nerves is novel and immensely interesting. What we question is the wisdom of allotting such a large share of the space to special topics. Perhaps this is once again only the carping criticism of the general surgeon who has seen such a narrowing of his field of endeavour; but it is just such experience that urges him to plead for a more general and a more balanced outlook in surgical teaching, and for a more rigid insistence on the indoctrination of the fundamental principles which are essential in every branch of practice.

In the preface we read that the " . . . book has been written primarily for undergraduate students. . . . Sufficient operative surgery has been included to meet the needs of those students intending to specialise in surgery". Even if we allowed this latter to be a proper objective (and we do not), we would still quarrel with this excuse to sanction the inclusion of the details of thymectomy, of the cleft palate operation and of the Denis Browne technique for the cure of hypospadias—and these criticisms can be applied in the general no less than in the particular.

If consideration of the shape, size and appearance of this book does not lead one to believe that it will be a best seller with the students, no more do its content and its argument hold promise of its favoured reception by his teacher.

Lung Function Tests: An Introduction. By B. H. Bass, M.D., M.R.C.P. (Lond.); 1958. London: H. K. Lewis and Company, Limited. 7¼" x 4¾", pp. 80, with 17 illustrations. Price: 8s. 6d. (English).

DR. BASS has succeeded in producing a simple primer of clinical pulmonary function tests for the clinician and senior student. On the whole he has avoided the main risks of over-simplification, of which he was aware, and there seems no need for him to attempt to appease the physiologists by addressing them with a capital P in his modest introduction. The work deserves to be widely read (it will be readily understood), and the following criticisms are offered in the belief that a second edition will be required.

The type of spirometer advocated is not ideal for recording rapid movements of the bell, and no kymograph should be purchased unless it can offer one speed of a centimetre or more per second. British and European work on the single-breath tests of ventilatory capacity and their joint efforts, with American approval, to standardize terminology in this field are largely neglected. The statement that "the timed vital capacity is probably the most instructive and useful test in use today" is a gross overstatement; further, the test is not "an excellent objective assessment" of obstructive lesions (if it was, it should be much more sensitive than it is to a good dose of a bronchodilator drug). The term "timed vital capacity" itself is misleading, and is not justified even on the grounds of priority, for the test was first described in France under another name. It is essentially a ratio, the significance of which can be properly assessed only in the light of the absolute values of its components. If this is done, errors of interpretation are avoided and much more information is gained—information which also solves Dr. Bass's difficulty in interpreting the results of the maximum breathing capacity in pulmonary fibrosis and other conditions causing a restrictive rather than an obstructive ventilatory defect. Indeed, if the absolute values are considered, Dr. Bass's first generalization is certainly true, and the second more nearly so. There is no mention of the comparatively poor repeatability of the maximum breathing capacity test and of its dependence on respiratory rate, factors which have led many British and European centres to discard it in favour of the more fundamental procedure of estimating the forced expiratory volume at (usually) one second. Walking ventilation is a poor second to the ventilatory response to a more severe exercise as a functional test; the latter is especially valuable when the lungs are "stiff" for any reason, or in suggesting the presence of alveolo-capillary block. Most of the various derived indices are redundant if the results of this test are considered together with the absolute and relative values obtained by the simpler ventilatory tests.

The method of estimating apparatus dead space seems out of place in a work of this kind, and the description of the Darling method of estimating functional residual capacity might well be replaced by a consideration of a better index of intrapulmonary mixing efficiency based on the helium method.

Commendably, fluoroscopy is described as a means of estimating pulmonary function; but the importance of this section is reduced by the suggestion that the routine radiograph "can, however, be of value in reaching some assessment of pulmonary function". This statement merely perpetuates an all-too-popular fallacy; but perhaps Dr. Bass meant merely that one should think in terms of the possible functional effects of a radiological lesion. Differential bronchospirometry is not a "very specialised technique"; its wide use and its appeal to surgeons justify some further consideration of its role and the indications for it. The final chapter adds little of value to the work; with some rearrangement it could well be replaced by a few clinical examples. It is a tragedy that a book of this type should appear without a solitary reference for more detailed reading; at least the more important review articles in each field should have been included.

The book is well produced and moderately priced. It deserves to succeed in disposing of the view that lung function tests are too complex and confused to be used and interpreted effectively by clinicians themselves.

Acetophenetidin: A Critical Bibliographic Review. By Paul K. Smith, Ph.D.; 1958. New York and London: Interscience Publishers. 9¼" x 5¾", pp. 192, with seven tables. Price: $5.75.

THIS monograph is the fourth in a series of five reviews of the literature on analgesic and sedative drugs. The previous volumes dealt with acetanilide, the salicylates and antipyrine. This is a valuable series for presenting together the scattered literature in this field.

Phenacetin, as this drug is usually called here, was introduced into medicine in 1887 as an antipyretic, and the amount consumed today must be exceeded only by aspirin. The book is composed of 12 chapters dealing with all aspects of the pharmacology of acetophenetidin in its broadest sense. After an historical survey, the author gives the physical and chemical properties, methods of estimation, metabolism, fate and excretion and analgesic and antipyretic actions, and concludes with a review of the therapeutic uses and toxicology. A bibliography of 529 references is appended, which must represent an appreciable number of the total papers on this drug. Each chapter carries a fair amount of detail, but perhaps is deficient, as are so many reviews, in its critical nature, since quite a number of very trivial observations are included.

In a summary at the conclusion of the monograph the author takes a more critical stand, and gives an excellent account of the general pharmacology of acetophenetidin which is sufficient for most purposes. He points out the established value of acetophenetidin as an antipyretic, but seems a little disturbed that proof of the analgesic efficacy in experimental animals is less certain. It is usually accepted now that drugs of this type are effective in pain associated with inflammation or capillary permeability changes. It is also probable that these drugs act peripherally, and so contrast with the narcotic analgesics, which have a marked central sedative action.

The book is a useful review for the professional pharmacologist, but is too specialized to be of wider interest.

The Comparative Anatomy and Physiology of the Nose and Paranasal Sinuses. By Sir Victor Negus, Hon. D.Sc., M.S., F.R.C.S. (England), Hon. F.R.C.S. (Edin.), Hon. F.R.C.S. (Ireland); 1958. Edinburgh and London: E. and S. Livingstone, Limited. 9¾" x 6¾", pp. 419, with 178 illustrations. Price: 70s. (English).

IN this book the many uses of olfaction, the most primitive of special senses, are enumerated. Birds make little use of olfaction, relying on vision. The same use of vision, to the suppression of olfaction, is seen in the arboreal mammals.

Olfactory mucosa, with its specialized cells of primitive origin, shows little variation throughout the animal kingdom. The snout enables such as the anteater to identify food by smell without seeing it. The high epiglottis of some species, which closes the naso-pharyngeal gap, maintains the integrity of the olfactory sense, when the mouth is open, during feeding. The direction of the air-stream and the air currents in relation to the turbinal systems in various species are considered.

The importance of the nose as an air-conditioning mechanism is discussed in detail, and in relation to the necessity of maintaining adequate humidity or olfaction. The minute anatomy of the nasal mucosa is described. An interesting chapter is devoted to Jacobson's organ, and its olfactory nature is confirmed. Ciliary action throughout the respiratory tract is discussed at length, and two chapters cover the wide field of tissue fluids and fluid balance. The prime reason for the existence of a nose is olfaction, and this point is underlined throughout the book. In higher apes and man, regression of the air-conditioning system with contraction of the mucosal area is associated with diminution of the olfactory sense.

The second part of the book describes the comparative anatomy of the paranasal sinuses in logical manner, with many illustrations. The author differs from Proetz in his account of the functions of the nasal sinuses. Comparative anatomy indicates that the sinuses exist to provide increased turbinate area. With diminution of olfaction and decrease in turbinates, the sinuses in man are regressive structures. In the same way the ethmoid cells, peculiar to man and the higher apes, have followed the decrease in olfactory space.

An appendix recapitulates the author's earlier work on the larynx, and a lengthy bibliography is given. This book is perhaps less easy to read than "The Mechanism of the Larynx", but this is because the subject is more diffuse. It is a masterly contribution to rhinology.

Muir's Text-Book of Pathology. Revised by D. F. Cappell, C.B.E., M.D., F.R.F.P.S., M.R.C.P., F.R.S.Ed.; Seventh Edition; 1958. London: Edward Arnold (Publishers), Limited. 9" × 6", pp. 1224, with 733 illustrations. Price: 70s. (English).

SEVEN YEARS have elapsed since the last edition of this book was published, and the new production maintains the high standard of its esteemed forebears. Rarely does a standard textbook appear with such a wealth of up-to-date information, and this feature is one which makes the new edition so welcome.

Much new material has been incorporated, and subjects such as keratoacanthoma, effects of irradiation, auto-immunization and collagen diseases are now included, whilst a few less important paragraphs have been deleted. This modernization has necessarily lengthened the text by some 110 pages; the illustrations have also been increased by nearly 100, and some of the old blocks replaced by new ones. Many sentences have been reconstructed and unnecessary words eliminated, so that the text becomes more readable. Likewise, there has been a good deal of rearrangement of the subject-matter, a more logical sequence being thus achieved. This is especially obvious in the chapter on tumours, which in previous editions was notoriously difficult to understand, especially for the undergraduate.

Throughout the text, increased emphasis is laid on physiological and biochemical aspects of disease, and this has required whole chapters to be practically rewritten. This applies particularly to renal function, in which aldosterone now receives proper recognition, and to the endocrine glands in general.

It is difficult to find any features that warrant serious criticism. Only two misprints could be found in the whole of the text, and the name of only one author (Dejerine, page 1027) was misspelt. There is throughout a rather liberal use of the term "recent work", and in one instance (page 352) the same term was used in the 1936 edition; this actually refers to a paper published in 1924. There are still some rather odd omissions. Why, for instance, does the alimentary system begin at the œsophagus and the respiratory system at the larynx? It might be asked, to what system do the mouth, the nose and the paranasal sinuses belong? It is a pity, too, that an occasional out-moded concept, such as the importance of silica in the development of coal workers' pneumonoconiosis, is perpetuated.

For two generations this celebrated work has been the standard textbook for medical students throughout the British Commonwealth (excepting, perhaps, Canada), and there is no doubt that this latest edition will maintain its unquestioned popularity. Furthermore, because of its modernization and the incorporation of such a wealth of new material, it is now a most desirable book for any post-graduate students studying pathology. Finally, it goes without saying that no teacher should be without it.

A Textbook of Fractures and Related Injuries. By J. Grant Bonnin, M.B. B.S. (Melbourne), F.R.C.S. (England); 1957. London: William Heinemann (Medical Books), Limited. 8¾" × 6", pp. 722, with 775 illustrations. Price: 84s. (English).

THIS book is essentially an expanded form of the earlier "Complete Outline of Fractures" published some years ago.

The information covers a wide field in a sound manner, and with that clear tabulation which always appeals to the senior or junior student. Indeed, the purpose of the book is shown by the inclusion of an appendix giving advice on the method of answering examination papers, and followed by sample questions.

There are full chapters on cerebral injuries and jaw fractures written by associates.

The chapter on ankle fractures is full of detail, and goes beyond the restricted range of the remainder of the book; it is worth reading.

The illustrations are numerous, and of better quality than those of the earlier work. However, it is regrettable that space is wasted in illustrating a mediæval method such as "well leg traction"; and the picture of a dislocated hip being reduced at floor level under "rag and bottle" inhalant anæsthesia bears no relation to modern methods using intravenous anæsthesia assisted by relaxants.

It is fitting that a Melbourne graduate should make reference to the "Hamilton Russell" method of leg traction; this has a more familiar ring to us than the surname alone.

This is a useful book for its intended users.

Books Received.

[The mention of a book in this column does not imply that no review will appear in a subsequent issue.]

"Gynecololgic Endocrinology", by G. M. Riley, Ph.D.; 1959. New York: Hoeber-Harper Book. 10¼" × 6", pp. 350, with illustrations. Price: $8.50.

A presentation of "the fundamentals of reproductive physiology, the endocrine aspects of gynecologic dysfunction, and details of useful diagnostic procedures".

"The Ætiology of Infective Diseases: With Special Reference to the Subsidiary and Important Nonspecific Factors", by Reginald Lovell, D.Sc. (Manchester), Ph.D. (London), M.R.C.V.S., D.V.S.M., 1959. Michigan: State University Press. Sydney, London, Wellington and Melbourne: Angus & Robertson, Limited. 5¾" × 8", pp. 136. Price: 33s. 3d.

The substance of a series of lectures given in the Department of Microbiology and Public Health at Michigan State University in 1955.

"The Radiation Reaction in the Vaginal Smear and Its Prognostic Significance: Studies on Radiologically Treated Cases of Cancer of the Uterine Cervix", by Olle Kjellgren. *Acta Radiologica*, Supplement 168; 1958. Stockholm: Acta Radiologica. 9¾" × 7", pp. 170, with 26 illustrations, 1 colour-plate and 31 tables. Price: Sw.Kr. 35.

The aim of the author was "cytologically to study the radiation reaction in the vaginal smear and to estimate the sources of error affecting its evaluation in a series of unselected patients undergoing primary radiation treatment for cancer of the uterine cervix".

"Geographic Ophthalmology: Asia, Australia and Africa", edited by William John Holmes, M.D.; 1959. Springfield, Illinois, U.S.A.: Charles C. Thomas, Publishers. 9" × 6", pp. 296, with many illustrations. Price: 63s. (English).

This book was "conceived as a reference for practising ophthalmologits and scholars dealing with common eye diseases found in tropical, subtropical and arid areas of the world".

The Medical Journal of Australia

SATURDAY, SEPTEMBER 5, 1959.

BREAKING THE COMMUNICATION BARRIER.

SPECIALISTS in most fields, but particularly those trained in a scientific discipline, often find it difficult to communicate their subject to those who are not so trained. With the physical sciences and the general run of biological sciences, this problem of communication is, or need be, only an intellectual one, involving the interpretation of terminology and the grasping of new concepts. With medicine, more often than not, there is an additional problem—the subjective interest of the layman in the matter to be communicated, which can bedevil the whole situation. Nevertheless, even here the basic problem is that of breaking the communication barrier.

Is it desirable or necessary to bother about popular science or popular medicine? On whether it is desirable opinions are sharply divided, but a strong body of opinion agrees, even if reluctantly, that it is necessary. The days of the oracle or of the initiate's exclusive rights to his mysteries have gone. This change is good in so far as it helps to dispel superstition and exposes the quack and the humbug. But the rapidly increasing complexity and power of science and of medicine lend increasing point to the danger of a little learning; and it seems better that the man in the street, not unreasonably curious about modern ideas and developments, should be informed from the best sources. Informed he will be, in any case; so there is a certain duty to help him avoid the shoddy and second-rate. It is important too to maintain his interest and goodwill towards science and scientific research if it is to command his support. Indeed, he has every right to know what is going on if he is expected to contribute financially either directly or indirectly.

In the broad scientific field this need to tell the general public has been long recognized. It was the purpose for which the British Association for the Advancement of Science was founded in the early part of last century; and although this purpose was long lost sight of, it is again being emphasized. The question was fully discussed last year in an editorial article in *Nature*,[1] which pointed out that the British Association was "not in the academic sense a learned society but rather a teaching and promotion organization". It appears that the Association has in the last year or two been making a firm and thoughtful effort to resume this role in the light of the outlook of the general public today, taking up the challenge well expressed by *The New Scientist* (quoted in the *Nature* editorial):

> Unity among scientists is essential—but it is not enough. Equally important is the interpretation of science to laymen so that they can intelligently insist upon its discoveries being used for the benefit of mankind. . . . This can only be done with any degree of success in a community which is so educated and informed that it is eager to listen and able to comprehend what the scientists are talking about. It cannot be done by merely introducing more teaching about science and its background, aims and objectives in our schools and then sitting back. On leaving school, our young people go out into a world of high-powered promotion, advertisement and indoctrination. . . . Recognizing that such heavily promoted attractions [such as entertainment, sport, high-pressure salesmanship, and even politics] may always be with us, science cannot afford to sit on the fence. It must enter the lists with its own promotion and continue plugging it long after schooldays are past.

A similar challenge was issued to the Australian and New Zealand Association for the Advancement of Science by Sir Mark Oliphant in his presidential address at last year's meeting.[1] He said that a primary purpose of A.N.Z.A.A.S. was "to improve the public appreciation of science and of its effects on society", but he feared that its congresses were becoming gatherings of specialists and that the journal it published was a journal only for scientists. "It may well be", he continued, "that in these critical days we should change our course and place greatest emphasis on the very difficult task of informing the layman of the true significance of the scientific method, of the power of its application to human problems and of the dangers of its misuse." What A.N.Z.A.A.S. does about this is its own business, not ours, but we shall be interested to watch any developments that take place. The British Association has apparently been rather disappointed at the initial response to its efforts.[2] The attendance at the annual meeting of the Association in Glasgow in August, 1958, was less than had been hoped for, as was the interest shown in certain innovations that were commendably imaginative. However, it will probably need a good deal of patience, persistence and experiment to find the most effective approach.

It must be admitted, of course, that there are very real, some would say insuperable, difficulties. The selection of material that is suitable for lay consumption is full of pitfalls, and there always remains the task of breaking the communication barrier. M. W. Thistle[3] considers that very little of what scientists know can get through to the layman; and as he is chief of the Public Relations Office of the National Research Council of Canada, he should know. He sees not one barrier to be broken, but a series of barriers. The first barrier is that of putting "things-going-on" into words in the first instance. The second is that of language and sophistication: translating from the language of scientists to the language of non-scientists and crossing the barriers of the various stages of scientific sophistication (a concept of a Sorbonne professor which we cannot stop to consider further now, but which Thistle discusses in a manner both entertaining and illuminating). The third is security—the variety of reasons (not only

[1] *Nature*, 1958, 181:1 (January 4).

[1] *Aust. J. Sci.*, 1958, 21:P8 (November).
[2] *Times*, September 1, 1958.
[3] *Science*, 1958, 127:951 (April 25).

military) why it is not expedient to pass on certain information. The fourth is printability—acceptability to the Press, which believes it knows what the public wants. The fifth is "what gets in"—what actually is read and then "reaches home in the brain of the reader". Thistle estimates that what finally gets through the five barriers is of the order of one ten-thousandth part of what the scientists know. This, he concedes, is still a fair amount, but communicating it has been hard work. In the long run, he suggests, the technique of successfully "breaking through the barriers and talking to ordinary folk about extraordinary things" is that of the master teacher Jesus—the use of analogy, comparison, metaphor, simile and parable. Another vital aspect of the approach is that stressed by John Pfeiffer[1] in a comment on Thistle's article—the simple duty of showing plain everyday courtesy to the reader. Without it we cannot hope to get far. With it a lot of apparently formidable problems can fade away. Nevertheless, the task of communication will never be easy, and for this reason we may the more admire Sir Mark Oliphant's Arthur E. Mills Memorial Oration published in this issue (see page 305), as a remarkably lucid exposition of modern physics for an audience composed almost entirely of laymen in that field. It provides an example and an encouragement to doctors faced with the somewhat different but still difficult task of passing on medical information, a subject that warrants separate discussion on another occasion.

Current Comment.

TOXICITY OF UREA IN URÆMIA.

It has long been believed that urea is non-toxic, and that the high concentrations in the blood in uræmia are harmless and contribute nothing to the symptoms present. The blood of elasmobranch fishes contains about 2% of urea, it being there to raise the osmotic pressure; if it is harmless to the fish it should be harmless to man. This, however, is a poor argument. E. F. Grollman and A. Grollman[2] have demonstrated that in high concentrations urea is toxic in dogs, and that many of the abnormalities seen in uræmia could appear after the administration of large doses of urea. The method of examination was to give intermittent peritoneal lavage with a solution of urea to nephrectomized dogs in sufficient amount to maintain the desired level of urea in the body fluids. The animals were kept alive and under observation for four to nine days. Symptoms of intoxication were apparent clinically in two to four days after the beginning of urea administration, at which time the urea content of the blood was 370 to 480 mg. per 100 ml. The first symptoms noted in the dogs were weakness, anorexia and inertia, their state being in marked contrast to that of dogs kept at a low blood urea content. Vomiting soon followed and persisted, with diarrhœa as a final symptom. The body temperature fell slowly until death. The animals finally went into a deep coma. At death the tissue water of all the body tissues showed a high concentration of urea equal to or slightly greater than that in the blood serum. Dogs who had had their kidneys removed, and who received intermittent peritoneal lavage with fluid without urea, could be maintained in apparently normal condition for several months except for the development of hypertension. Since the only variable introduced in the dogs given urea was the high urea content of the tissue fluids, the uræmic symptoms can be attributed only to the elevated urea level. Not all the symptoms of uræmia were seen in these dogs, so that other factors are involved in the development of uræmia during renal insufficiency. The concentrations of urea used in these experiments were high, but symptoms have been obtained when the concentrations of urea have been such as those met with clinically. The parallelism of the development of symptoms in the experimental dogs and clinically in man was very close. That urea in high concentration is toxic in the animal body is not surprising when one considers the direct action of urea on proteins and the disruption of enzymes which it causes.

[1] *Science*, 1958, 127: 955 (April 25).
[2] *J. clin. Invest.*, 1959, 38: 749 (May).

CHLOROTHIAZIDE AND HYDROCHLOROTHIAZIDE.

THE use of chlorothiazide as a diuretic was discussed in these columns on October 18, 1958, and comment was also made on its hypotensive action. Since then numerous reports have appeared, in general confirming the claims made in earlier papers. Most difference of opinion is seen in relation to its hypotensive action and the cause of this action. The latest paper on this subject is by C. T. Dollery, M. Harington and G. Kaufmann,[1] with the title "The Mode of Action of Chlorothiazide in Hypertension with Special Reference to Potentiation of Ganglion-Blocking Agents". They found that single intravenously administered doses of chlorothiazide had no appreciable effect on the blood pressure or on the hypotensive response to a standard intravenously administered dose of the ganglion-blocking drug pentolinium. After chlorothiazide had been given by mouth for three days, an increased sensitivity to pentolinium developed in nine out of 13 patients. This was found to correlate with reduction in plasma volume caused by the chlorothiazide, and the effect was abolished after "Dextran" infusion. This diminution in plasma volume is thought by Dollery, Harington and Kaufmann to be one of the main factors in the increased effect of ganglion-blocking drugs in patients treated with chlorothiazide.

Recently hydrochlorothiazide has been introduced. This differs from chlorothiazide in having two hydrogen atoms introduced into the molecule to saturate one of the double bonds. Several workers have shown that weight for weight this new compound is very much more active than chlorothiazide. P. R. Fleming, J. F. Zilva, R. I. S. Bayliss and J. Pirkis[2] have made a comparison of the effects of chlorothiazide and hydrochlorothiazide. The two drugs were given to four patients fully convalescent from conditions unaccompanied by œdema, to two other convalescent patients and to six healthy ambulant subjects. The diuretic effects of the two drugs appeared in each case about two hours after the drugs were taken, and determination of the relative potencies indicated that 25 mg. of hydrochlorothiazide were equal to 0·5 gramme of chlorothiazide; that is, the hydrochlorothiazide is about 20 times more potent than chlorothiazide in convalescent patients and normal subjects. In patients with œdema this relation did not always apply, and more patients showed a 1:10 ratio; the cause of this is not yet clear, but it may be related to better intestinal absorption. Hydrochlorothiazide did not promote the excretion of bicarbonate to the same degree as did chlorothiazide, but there was little difference in the potassium excretion with both drugs. It is to be remembered that potassium excretion is one of the things which have to be watched closely in administering chlorothiazide.

D. V. S. Kerr, A. E. Read and S. Sherlock[3] have studied the effects of hydrochlorothiazide in the control of ascites. They found that 500 mg. of chlorothiazide and 50 mg. of hydrochlorothiazide were equivalent doses in most cases, but not always. This, of course, is of no

[1] *Lancet*, 1959, 1: 1215 (June 13).
[2] *Ibid.*, 1959, 1: 1218 (June 13).
[3] *Ibid.*, 1959, 1: 1221 (June 13).

particular value to the patient if the diuretic effect of the two drugs is essentially the same, as they found. As the new drug has no less tendency to cause serious potassium depletion than chlorothiazide, the same care must be taken with the administration of both drugs, particularly if liver disease is present.

There seems then from these findings to be no advantage in giving hydrochlorothiazide instead of chlorothiazide, unless it be that, because less of the new drug is required, treatment with it should be cheaper.

THE SOURCES OF AMNIOTIC FLUID.

Most textbooks have little to say about the source of the amniotic fluid, and this is partly because there was, until comparatively recently a signal dearth of accurate information on the subject, so that views as to the origin of the fluid were largely speculative. Therefore, when G. J. Vosburgh and his colleagues[1] reported the results of studies on the transfer of radioactive isotopes into and out of the amniotic cavity, their observations appeared as filling a blank space in existing knowledge, and they have strongly influenced subsequent opinions on this subject, especially as their results appeared to be supported by those of other workers. However, in a recent paper by T. N. A. Jeffcoate and J. S. Scott[2] the conclusions drawn from Vosburgh's findings are questioned. Vosburgh and his colleagues had concluded that the liquor amnii was completely exchanged every three hours. Jeffcoate and Scott point out that this quite obviously does not agree with the clinical behaviour of women who sustain rupture of the membranes during pregnancy but do not immediately go into labour; they do not lose fluid at the rate of two to three pints every three hours. They note that Vosburgh's results on the rate of water exchange refer to only five subjects, at various stages of pregnancy, and that the rate of renewal usually quoted is an average of five widely different and not strictly comparable results. Further, Vosburgh's data on sodium exchange indicated a rate of turnover only one-fifth that of water. Jeffcoate and Scott conclude that the most important contribution made by radioactive isotope studies is the clear demonstration that the pool of liquor is not a static reservoir, but that both the fluid and its chemical contents are in a state of continual flow, though the volume of liquor remains fairly constant for each stage of pregnancy. The normal volume and pathological variations from it are likely to be determined by the relative efficiency of the mechanisms for production and disposal.

In a paper written ten years ago, in which they discussed the origin of the amniotic fluid, R. E. Shaw and H. J. Marriott[3] mentioned four theoretically possible sources of the fluid: (i) active secretion by amniotic epithelium; (ii) passive transudation from the maternal circulation; (iii) passive transudation from the fœtal circulation; (iv) fœtal urine. They concluded that amniotic fluid was mainly a secretion of the amnion, but that, at least in some cases, fœtal urine made a significant contribution. They also stated that the problem was clearly far from solution, and they were apparently unaware of the transient nature of the fluid. Jeffcoate and Scott usefully insist that each phase of pregnancy should be considered separately, because there is much evidence that the rates of formation and removal of liquor amnii change with the progress of pregnancy. Its dissolved constituents certainly do. They point out that the fœtal kidneys are capable of some function by the twentieth week, and suggest that up to this stage liquor amnii is derived almost entirely from the amnion, either by secretion or by transudation, but that after mid-pregnancy the fœtal kidneys are an additional and perhaps even more important source of supply. It should be recognized that the composition of the fœtal urine differs from that excreted after birth, and varies according to the stage of pregnancy.

In discussing the disposal of the liquor amnii, Jeffcoate and Scott point out that the amnion may absorb as well as secrete fluid, and that the possibility must be conceded that it plays some part in the return of the various components of the liquor to the maternal circulation. They refer briefly to the possible roles of the fœtal skin and respiratory system, indicating that these are not likely to be of much significance. However, they regard the fœtal alimentary tract as the main route by which the fluid is returned to the maternal circulation, quoting in particular the results of one investigation, in which inulin was used as a tracer substance, and in which it was calculated that the fœtus swallows 500 ml. of liquor amnii every 24 hours.

In another part of their paper Jeffcoate and Scott consider the evidence derived from polyhydraminos and oligohydraminos. It has long been known that anencephaly is frequently associated with polyhydramnios, and Jeffcoate and Scott show that out of 169 consecutive cases of hydramnios seen at one hospital, one-third were associated with some condition which prevented the fœtus from swallowing; the two commonest of these conditions were anencephaly (32 cases) and œsophageal atresia (12 cases). In the other two-thirds no causal mechanism for polyhydramnios could be demonstrated, but interesting observations are quoted to indicate some of the other mechanisms which could be responsible. In cases of oligohydramnios there is a high incidence of renal agenesis. Since oligohydramnios may often pass unnoticed, it is more profitable to regard this association from its reverse aspect. From their own experience and from the literature Jeffcoate and Scott assemble 295 cases of renal agenesis or severe dysplasia. There was firm or presumptive evidence of oligohydramnios or anhydramnios in 100 of these, and in the great majority of the remainder there was no statement as to the amount of liquor present. A small number of such cases have been reported in which liquor was present in normal or excessive amounts, and one such case occurred in their own series; in this case iniencephaly was also present, a condition otherwise known to be associated with polyhydramnios, presumably on account of interference with fœtal swallowing. This one exception in their series therefore suggests that polyhydramnios associated with renal agenesis may be explained by the presence of some additional defect which interferes with the disposal of fluid of non-renal origin, and does not invalidate the basic hypothesis. Jeffcoate and Scott state that they have only recently come to support the view that deficiency of liquor is rare except in association with bilateral renal agenesis or obstruction of the urethra, but that in the last 5000 deliveries at one hospital with which they were associated there were six proved cases of oligohydramnios; in three of these renal agenesis was also present; in the remaining three the renal tract was normal, but in each there was a history of threatened abortion early in pregnancy, and at delivery large areas of the membranes were covered on the maternal aspect by organized blood clot. Such lesions could have hindered the transfer of fluid through the membranes, suggesting that the cause of oligohydramnios in these cases was failure of the amnion to contribute its quota to the total volume of liquor.

In conclusion Jeffcoate and Scott state that there is clearly no simple solution to the problem of the origin and fate of liquor amnii. They consider that it seems certain that each function is covered by more than one mechanism, and that the relative importance of different mechanisms changes with the progress of pregnancy. Finally, they make some suggestions as to how the findings of the experimentalists may be reconciled with clinical experience, and point out that, whether or not this reconciliation is valid, well-documented clinical events cannot be ignored merely because they do not tally with experimental findings. The evidence so ably marshalled by Jeffcoate and Scott appears to be a valuable contribution towards restoring some degree of perspective in this complex subject.

[1] *Amer. J. Obstet. Gynec.*, 1948, 56: 1156 (December).
[2] *Canad. med. Ass. J.*, 1959, 80: 77 (January 15).
[3] *J. Obstet. Gynæc. Brit. Emp.*, 1949, 56: 1004 (December).

Abstracts from Medical Literature.

OPHTHALMOLOGY.

Corneal Epithelial Changes during Chloroquine Therapy.

L. L. CALPINS (*A.M.A. Arch. Ophthal.*, December, 1958) reports on seven patients under treatment with chloroquine who suffered ocular complaints. Variable doses of chloroquine had been employed for a variety of clinical entities. Those receiving larger doses developed symptoms earlier than those on small doses. There was diffuse haziness of the epithelial and subepithelial layers of the cornea. In some, there were local increases in density resembling vercillate dystrophy. The stroma was not involved. All patients became markedly improved or completely free of symptoms upon discontinuing the drug. The chief complaint was blurred vision outdoors, and in some there was a complaint of haloes. The visual acuity on the Snellen chart was not materially altered. The corneal changes are similar to those described as occurring in patients receiving quinacrine ("Atebrine").

Malignant Glaucoma.

A. G. GROSS (*Brit. J. Ophthal.*, January, 1959) describes the cure of a patient with bilateral malignant glaucoma without removal of the lenses. Under general anæsthesia a cyclodialysis was performed, combined with posterior sclerotomy and vitreous evacuation, and the filling of the anterior chamber with air through the cyclodialysis track. Reformation of the anterior chamber with air is an essential procedure.

Keratoplasty for Fuchs's Dystrophy.

R. T. PATON AND G. SWARTZ (*A.M.A. Arch. Ophthal.*, March, 1959) report on their experiences of keratoplasty for Fuchs's dystrophy. Twenty-three keratoplasties were performed on 20 eyes. In 22 cases partial penetrating grafts were used, including 19 of 6 mm. and three of 7 mm. diameter. In one case a 7 mm. lamellar graft was used. Clear grafts were obtained in 14 of the total series of 20 eyes. Results in eyes with early or moderate disease, however, were strikingly better than results with advanced dystrophy. Cataract is a frequent complication of Fuchs's dystrophy, and in this series cataract was present in 12 of the 20 eyes.

Cataract Cases Lost Before Surgery.

W. H. HAVENER (*Amer. J. Ophthal.*, February, 1959) lists the causes of preventible complications in cataract surgery as infective, allergic, degenerative, traumatic, congenital, neoplastic, systemic and psychological. Chronic dacryocystitis, marginal blepharitis and acute infections are contraindications to surgery. Routine instillation of antibiotics for 24 hours before surgery reduces operative infection. Uveitis and drug allergies are the allergic factors. Where uveitis is present, surgery must be deferred until the eye has been quiet for some months. Of the degenerative conditions which will prevent a satisfactory result, the author mentions Fuchs's endothelial dystrophy, chorio-retinal degeneration, macular degeneration, optic atrophy, neovascularization of the iris and retinal detachment. Advanced malignant melanoma should be considered in the presence of unilateral cataract. A short palpebral fissure may make surgery difficult, and previous amblyopia ex anopsia is a contraindication to surgery. The presence of old injuries may militate against success, and self-inflicted injury at and after operation must be guarded against. Premature cataract extraction may produce an unhappy patient. Many psychological problems will not occur if surgery is postponed.

Serum Sodium and Potassium Levels in Glaucoma.

P. DESVIGNES AND M. KOPILOFF (*Presse méd.*, February 28, 1959) have investigated the serum sodium and potassium levels in 34 cases of acute, subacute or chronic glaucoma. They found that the sodium level was unaffected, whilst that of potassium was reduced. They express surprise at this result, since the administration of acetazolamide, which lowers intraocular tension, produces a diminution of the potassium concentration in the plasma as well as in the aqueous humour. They conclude that disturbances of sodium and potassium concentrations are not involved in the ætiology of glaucoma.

Ocular Manifestations of Internal Carotid Artery Occlusion.

N. GORDON (*Brit. J. Ophthal.*, May, 1959) discusses the ocular signs of internal carotid occlusion and describes the findings in 10 patients. The two commonest ocular symptoms are blindness of the homolateral eye and hemianopic field defects. The unilateral blindness may be transient or permanent. Homonymous hemianopia may be transient but is usually permanent. Pupillary abnormalities and external ocular muscle palsies occur occasionally. The author discusses the manner in which the signs and symptoms are produced.

Experimental Trachoma Produced by Cultured Virus.

L. H. COLLIER *et alii* (*Brit. J. Ophthal.*, December, 1958) describe the successful inoculation of a human volunteer with trachoma virus. The volunteer had had both eyes removed for secondary glaucoma. The tarsal conjunctiva of the left upper lid was inoculated with infected yolk sac suspension. The right eye was treated with normal yolk sac suspension. The patient was observed for 219 days. The typical clinical and histological picture of trachoma was produced, with the development of inclusion bodies, and the virus was recovered from the conjunctiva.

Ataractic and Antiemetic Drugs in Cataract Surgery.

R. D. HARLEY AND J. E. MISHLER (*Amer. J. Ophthal.*, February, 1959) attempt to evaluate the usefulness of chlorpromazine ("Thorazine"), prochlorperazine ("Compazine") and perphenazine ("Trilafon") in 250 consecutive cataract extractions. The first 100 patients had the following routine: 100 mg. of pentobarbitone ("Nembutal") given the evening before operation, and repeated four hours before and again one hour before operation; 50 to 100 mg. of pethidine and 50 mg. of dimenhydrinate ("Dramamine") given one-half hour before operation; 50 mg. of pethidine given every four hours after operation, for pain. The second 100 patients had identical pre-operative orders with the addition of chlorpromazine 25 mg. given orally one-half hour before operation. Chlorpromazine 25 mg. was given parenterally immediately after operation and again every three hours if necessary. An additional series of 25 cases received the identical treatment except that "Compazine" 10 mg. was substituted for chlorpromazine. A fifth series received 4 mg. of "Trilafon", the other pre-operative and post-operative treatment being as before. All three drugs had an impressive therapeutic effect on the tense and apprehensive patient. Chlorpromazine was judged to be the most potent sedative. All three drugs have pronounced antiemetic properties. Chlorpromazine potentiates depressant drugs such as the barbiturates, whereas "Compazine" and "Trilafon" exhibit a low order of potentiation.

Intracapsular Cataract Extraction using Alpha-chymo-trypsin.

J. E. H. COGAN *et alii* (*Brit. J. Ophthal.*, April, 1959) report on the use of alpha-chymo-trypsin in 122 cataract extractions. In 72 cases extraction was by means of the erysophake and in 50 cases with the use of intracapsular forceps. The authors are of the opinion that the removal of senile cataract is made easier with this enzyme and its use causes no damage to intraocular structures. They state that they are so impressed by the ease with which the lens is removed that they would not willingly operate without its use.

D. AINSLIE (*Brit. J. Ophthal.*, April, 1959) describes the use of alpha-chymotrypsin in 32 consecutive cases of cataract extraction. From this series the author was able to conclude that the enzyme is effective in reducing the strength of the zonule without damaging other intraocular structures. The author prefers forceps to the erysophake in extracting the lens.

E. L. ZORAS (*Brit. J. Ophthal.*, April, 1959) reports on the use of alpha-chymotrypsin in 26 cataract extractions. The author is of the opinion that in patients over 60 years the addition of the enzyme is of so little advantage as to be scarcely worth the extra manipulations involved. In the younger age groups it is of distinct advantage, allowing the lens to be delivered with ease. No deleterious effects on the eye were noted.

Prevention of Retinal Detachment in Cataractous Eyes.

A. CALLAHAN (*Amer. J. Ophthal.*, April, 1959) recommends prophylactic diathermy to a cataractous eye where the fellow aphakic eye has suffered retinal detachment. The procedure is indicated in eyes in which (*a*) idiopathic detachment has occurred in the fellow eye with or without cararact extraction, (*b*) peripheral cystic degeneration has occurred, or

(c) the eyes are highly myopic with evidence of choroidal or chorio-retinal stretching. A circular incision is made through the conjunctiva and Tenon's capsule between the insertions of the muscles. A line of diathermy punctures, 2 mm. apart, is made between the muscles 10 mm. from the limbus. Diathermy current is applied on the sclera beneath the tendons with a Rychner electrode. The conjunctiva is closed and cataract extraction is performed three months later.

Accidental Laboratory Infection with Trachoma.

C. H. SMITH (*Brit. J. Ophthal.*, December, 1958) reports a case of accidental infection with trachoma virus. The virus was recovered subsequently from each eye. The patient had been treated with "Aureomycin" locally and "Achromycin" by mouth, but marked clinical improvement did not occur until penicillin treatment had been commenced.

OTO-RHINO-LARYNGOLOGY.

Treatment of Papilloma of the Larynx.

F. C. W. CAPPS (*Ann. Otol. (St. Louis)*, December, 1957) states that as yet no specific therapy for papilloma of the larynx has appeared. Perhaps some form of chemotherapy or antibiotic therapy for the virus or viruses which may be responsible for the disease will ultimately replace present-day surgical procedures. Until such therapy is practical, the author suggests that the following list of "don'ts", compiled by his colleague, Dingley, will serve as guide-posts in the treatment of laryngeal papillomas: (i) "Don't attempt to give a child with a larynx full of papilloma a good voice; you will be very likely to give such a case a permanently bad adult voice." (ii) "Don't do both sides at one sitting." (iii) "Don't do more than pluck off the protruding papilloma." (iv) "If there are small papillomata on both cords up to the anterior commisure, leave this critical area alone." (v) "All treatment should have one aim—don't damage the larynx."

The Development of Modern Temporal Bone Surgery.

J. LEMPERT (*A.M.A. Arch. Otolaryng.*, May, 1959), in a discussion of the principles in the development of modern temporal bone surgery, begins with an historical résumé of the "greats" in otological surgery, from Petit, who in the 1750's operated successfully for suppurative mastoiditis, to Rambo, whose paper on "Musculoplasty, a new operation for suppurative middle ear deafness" was presented in April, 1958. He states that the incorrect concepts upon which the early otologists acted have led ultimately to the present state of affairs. The fundamental of drainage, today the underlying principle, was not really presented until Von Troeltsch's paper in 1861. The works on the anatomy and physiology of the region are recalled. Attempts to cure deafness were commenced as early as 1876, when attempts to correct the recognized ankylosis of the footplate of the stapes were attempted. This ankylosis had been reported as early as 1735 by Valsalva. These attempts were abandoned as inefficient and dangerous procedures. The author states that the basic underlying principle of restoration of hearing, whether in cases of otosclerosis or suppurative conditions of the middle ear and mastoid, is "remobilization of the inner ear fluids". In the infective cases he emphasizes the necessity of (i) removal of pathological lesions and (ii) reconstruction of a new, air-filled, middle ear space communicating with the nasopharynx. He comments upon the harm done by antibiotic therapy used alone, when it masks the true picture. The necessity of myringotomy is stated. Work on the surgical treatment of Ménière's disease is described and the proposition that the condition is viral in ætiology is presented. Finally the author comments on the recently revived operation for mobilization of the stapes. He considers it "a destructive, non-surgical orthopædic procedure with complete disregard for the biological and physiological factors upon which maintenance of the improvement will depend".

Acetazoleamide in Ménière's Disease.

G. V. VARGA AND O. RIBARI (*J. Laryng.*, November, 1958) discuss the action of acetazoleamide in the treatment of Ménière's disease. They treated 21 patients with undoubted Ménière's disease with acetazoleamide. Twenty of these patients became lastingly free from attacks, and 11 displayed marked improvement of hearing. Other subjective symptoms also exhibited considerable amelioration. In the authors' opinion acetazoleamide exercises in Ménière's disease a paralysing effect on carbonic acid anhydrase which is present in the labyrinthine fluid. In this way the excretion of electrolytes is greatly enhanced, thereby diminishing the osmotic pressure of the endolymph very greatly.

Otitis Externa.

R. D. STRIDE (*J. Laryng.*, January, 1959) presents a study of 230 cases of otitis externa among patients seen in Germany and Cyprus. Of interest is the different nature of the infecting organism in the two countries. *Staphylococcus aureus* proved to be the most common infecting organism in Germany, while *Pseudomonas pyocyanea* predominated in Cyprus. In both countries a significant number of cases possessed a similar staphylococcal infection of the nailfolds and nasal vestibules. An association was revealed between finger-nail neglect and otitis externa. Skin disorders and dandruff were present in one-third of cases. Hair washing was performed frequently but in an unsatisfactory manner. Swimming, as an ætiological factor in otitis externa, was supported by the findings in Cyprus. A source of fæcal contamination was observed. Over 40% of cases of otitis externa occurred within six months of arrival in the country. A high proportion of cases had a history of previous attacks. A seasonal variation in the incidence of otitis externa, although but little marked in Germany, was a notable feature in Cyprus, where it was closely associated with meteorological variations. Attention is drawn to inner-third meatal injection as an early physical sign of the disorder. Treatment cured 60% of patients in seven days or less, the results being obtained more quickly with in-patients. Recurrence occurred in less than 15% of all cases. Neomycin and hydrocortisone ointment proved of great value. Prevention included advice on keeping the ears dry, avoiding local trauma and maintaining a high standard of personal hygiene.

Penetration of Aerosols into the Nasal Sinuses.

R. GUILLERM *et alii* (*Presse méd.*, May 30, 1959) studied in dogs the penetration of aerosols into the accessory nasal sinuses, by means of a technique which they devised. They found that penetration was slight when the usual aerosols were employed, and set about devising a means of improving it. They found that the use of sound vibrations, strong enough to be transmitted by the air to the opening of the sinus, brought about rapid diffusion of the aerosol. The first traces of the aerosol appeared in the dog's frontal sinus in 20 seconds, whereas under normal conditions 30 minutes were required. The authors state that they are investigating the use of the method in the treatment of patients with sinusitis, and that it is likely to have other applications. They describe the method and apparatus in detail.

Idiopathic Recurrent Laryngeal Nerve Paralysis.

R. G. WILLIAMS (*J. Laryng.*, March, 1959), in discussing idiopathic recurrent laryngeal nerve paralysis, states that early writings suggested that approximately 50% of cases of recurrent laryngeal palsy were idiopathic. In the author's series this figure is 36%, which is in keeping with the figure of 33% in the series from the Mayo Clinic. It would seem that between 83% and 90% of the idiopathic cases make a spontaneous recovery. It has been stated that if there is no recovery in six months the outlook is probably hopeless. In the author's series the average time for recovery was five and a half months. In general, the hoarseness averaged one month less in duration. There were more males than females (46 to 20) in the series. The left cord was involved in 65% of cases.

Hæmangiomas of the Nose.

D. A. OSBORN (*J. Laryng.*, March, 1959) reports a study of a series of 51 cases of hæmangioma of the upper respiratory tract seen in a ten-year period. Over half of the cases occurred on the nasal septum, the next commonest sites being the lateral wall of the nasal fossa and the nasal vestibule. Macroscopically they appear as extremely vascular polypi. Microscopically they are typical capillary hæmangiomas. They occur more frequently in middle age, the main symptoms being epistaxis and nasal obstruction, which have been present, on an average, somewhat less than six months. The question of ætiology is discussed and the opinion expressed that they are not malformations as suggested by Wells, but truly benign neoplasms.

Brush Up Your Medicine.

INFECTIONS OF THE URINARY TRACT: BACTERIOLOGICAL ASPECTS.

URINARY tract infections must be regarded as those conditions in which bacteria are present in the kidney and urinary tract.

The route of infection may be (*a*) hæmatogenous, in which case bacteria reach the kidney by way of the blood-stream, or (*b*) ascending, by way of the ureter or periureteral lymphatics, or (*c*) possibly direct, from the intestines by way of lymphatics. Hæmatogenous spread is by far the commonest.

Bacteria may be present in the urine without pus (bacilluria) or with pus (pyuria). The presence of bacteria in the urine must imply some renal damage, as the kidney does not normally filter organisms.

Infection of the kidney may be caused by almost any organism, but those usually found are *Escherichia coli*, *Staphylococcus aureus*, *Streptococcus*, *Proteus vulgaris* and *Pseudomonas pyocyanea*. Infections of the cortex of the kidney are usually due to pyogenic cocci. Infections of the portions near the kidney pelvis and the pelvis itself are usually due to *E. coli*. In the lower part of the urinary tract, *E. coli*, *Ps. pyocyanea* and *Pr. vulgaris* are most commonly found, and generally these are associated with trauma or obstruction. Post-operative infection following surgical procedures in the urinary tract is most frequently caused by Gram-negative bacilli.

Infections of the urinary tract may be (i) pyelonephritis with sometimes necrotizing renal papillitis, (ii) pyelitis, (iii) cystitis, (iv) urethritis, (v) prostatitis, (vi) seminal vesiculitis and (vii) tuberculosis. Rarely actinomycosis and moniliasis of the urinary tract may occur.

Infections of the urinary tract are second only to infections of the respiratory tract in frequency. It is surprising therefore that the knowledge of the pathogenesis, incidence and natural history of pyelonephritis and related infections of the urinary tract is so incomplete.

In this contribution to this discussion on urinary tract infections, two aspects only will be stressed: the first, the importance of adequate laboratory investigation; the second, some aspects of treatment especially in relation to antibiotic therapy.

Laboratory Investigation.

Adequate laboratory investigation includes a full bacteriological and chemical examination of the urine and a chemical investigation of urinary function. It is important that there should be close cooperation between the ward and the laboratory in the collection and handling of specimens of urine. Catheter specimens are essential from the female and desirable though not essential from the male. Specimens are preferably collected first thing in the morning. This is better than random samples, as the urine which has stagnated in the bladder overnight has been allowed the longest incubation period. When tuberculosis is suspected, the specimen should be a catheter specimen collected first thing in the morning after restricted fluid intake. This is much better than the old-fashioned method of collecting a twenty-four hour specimen. Specimens for chemical examination may require certain special techniques.

It is of the greatest importance that the specimen, especially if it is for bacteriological examination, should be collected in a sterile container and kept free from contamination by the air or by dust. Too often the specimen is collected and left about uncovered. Contamination with air-borne or dust-borne organisms occurs, and subsequent bacteriological examination is rendered difficult if not valueless.

A full examination in the bacteriology laboratory should include a microscopic examination, aerobic and anaerobic cultures, antibiotic sensitivity testing of pathogens isolated and animal inoculation when necessary — e.g., in tuberculosis and leptospirosis. Examination for fungi is important, especially as monilial infections are now not uncommon. Parasites may be found.

There is some debate as to whether the microscopic examination should be carried out on a centrifuged or uncentrifuged specimen; surely this must depend on the nature of the lesion and on the reason for the examination. Many urologists prefer a report on an uncentrifuged specimen both initially and in follow-up, especially in infective lesions. It is held by them that in this way a more accurate estimate of response to therapy can be ascertained.

This would apply also in the follow-up investigation of a patient suffering from acute nephritis with blood in the urine. However, if the examination is for parasites or ova, a centrifuged deposit should be examined. When the report is given, the type of specimen examined should be stated in the report.

The symptoms, signs and abnormal urinary elements that occur in pyelonephritis are reactions to the presence of bacteria in the kidney. Bacteria may be present in quantity in the urine without pyuria or without symptoms. This emphasizes the insidious and chronic nature of many cases of pyelonephritis. The presence of bacteria in the urine is of more importance than the findings that are secondary to inflammation or renal damage.

The detection of bacilluria presents certain problems. If only a few contaminating organisms fall into the urine they will give rise to positive cultural findings. It has been found that multiplication of common pathogens in the urine is rapid and bacterial counts rise to 10^8 bacteria per millilitre in eight to twelve hours. Bladder specimens from patients with undoubted acute pyelonephritis nearly always have more than 10^5 organisms per millilitre. It may be assumed that bacilluria is present when bacterial counts are 10^6 or more per millilitre of urine. Counts below this probably indicate contamination. There are certain instances, however, in which the count may be below 10^6 bacteria per millilitre of urine even when active pyelonephritis is present; this may occur under the following circumstances: (i) When a bacteriostatic agent is present in the urine. (ii) When the rate of urine flow is rapid, the numbers of bacteria discharged from the kidney are small and pooling of the urine in the bladder for a long enough time to permit multiplication to significant levels has not occurred. It is for this reason that the early morning specimen is better than random samples. (iii) When urinary pH and dilution have limited the degree of bacterial multiplication in the urine. The urine should not have a pH below 5·0. Dilution effects become noticeable at a specific gravity of 1003. (iv) When certain organisms that grow poorly in urine are present — e.g., group A streptococci. (v) In ureteral obstruction; the bladder urine may be sterile in this condition.

Gram staining of the deposit should always be performed. This will serve to differentiate Gram-negative organisms. The Gram stain may give much valuable information, and may be a method of differentiating between contaminants and pathogens. However, the Gram staining must be interpreted very carefully.

If tuberculosis is suspected, it is essential that the urine be cultivated on suitable media and that animal inoculations be performed. It is of greater importance in urinary tract infections than in most other diseases that the animal inoculation be the final court of appeal.

Treatment.

Treatment must be a careful combination of removing the cause and suitable drug and/or antibiotic therapy.

Removal of the cause involves dealing with any obstructive lesion in the urinary tract, such as stricture, calculus or congenital abnormality; reducing the use of catheterization to a minimum; reducing the use of indwelling catheters to a minimum; the correction of debilitating diseases and gynæcological disorders.

Suitable drug therapy may be considered under the two headings of (i) non-antibiotic therapy and (ii) antibiotic therapy.

Non-Antibiotic Therapy.

The earliest attempts at medical therapy were directed toward rendering the urinary tract unsuitable for bacterial multiplication by inducing changes in pH and specific gravity. These were of limited value, because pH values below 5·0 are necessary to kill most of the common pathogens, and because extreme dilution of the urine inhibits bacterial multiplication but slightly. The discovery that beta-hydroxybutyric acid and a variety of other organic acids, including mandelic acid, inhibit bacterial multiplication in acid urine was a major advance in therapy. The use of ketogenic diets and acidifying salts gave way to mandelic acid. Most strains of the common urinary tract pathogens are inhibited *in vitro* by mandelic acid. *Aerobacter aerogenes* and *Pr. vulgaris* may be some-

what resistant. These older methods of treatment of urinary infections, when used properly, are highly effective in the treatment of most acute uncomplicated infections of the urinary tract. They are not very effective in chronic and complicated infections.

The value of sulphonamides in the treatment of urinary tract infections is well established. The sulphonamides show the same pattern of response to chronicity and anatomical lesions as do the older methods of treatment. They are, however, somewhat more effective.

Antibiotic Therapy.

With the development of antibiotics, the older methods of treatment were dropped and antibiotics were substituted. This had its disadvantages because antibiotic-resistant strains of organisms emerged, and often the antibiotics became valueless as therapeutic agents. The four organisms in which the emergence of antibiotic-resistant strains is a problem—namely, *Staph. aureus*, *E. coli*, *Pr. vulgaris* and *Ps. pyocyanea*—are frequently found in urinary tract infections. Therefore it is essential that there be adequate bacteriological control before and during treatment. Under proper conditions correlation is better than 90% between antibiotic sensitivity and elimination of bacteria from the urine. However, in chronic complicated infections reinfection and relapse rates are high, and the ultimate correlation does not exceed 10%.

All the various antibiotics—penicillin, streptomycin, tetracycline, chloramphenicol, novobiocin, polymyxin, bacitracin and neomycin—have been used either singly or in combinations. In staphylococcal infections the same problem of resistant strains presents as in staphylococcal infections in other systems. The problem of resistant strains of the Gram-negative bacilli is an increasing one. In a survey carried out at the Fairfax Institute of Pathology, Royal Prince Alfred Hospital, Sydney, the following results relating to resistance were obtained. Of 514 strains of *E. coli* examined 51·8% were resistant to streptomycin, 67·8% were resistant to tetracycline and 41·6% were resistant to chloramphenicol. Of 160 strains of *Pr. vulgaris*, 32·5% were resistant to streptomycin, 87·5% were resistant to tetracycline and 36·9% were resistant to chloramphenicol. Of 83 strains of *Ps. pyocyanea*, 53% were resistant to streptomycin, 92·8% were resistant to tetracycline and 83·1% were resistant to chloramphenicol.

Nitrofurantoin has proved very effective in the treatment of urinary tract infections. It is interesting to note that *Staphylococcus aureus* is nearly always sensitive to this drug.

Comment.

Although there is every possibility that susceptible bacteria will be cleared from the urinary tract by proper antibacterial measures, clinical control of the infection is largely dependent on the nature of the urinary tract lesion. There are three possible explanations why this should be:

1. Antibacterial therapy may have failed to eradicate the infecting organism completely, so that there is reinfection at a later date. This may occur in chronically infected kidneys and perhaps in acute uncomplicated pyelonephritis.

2. Antibacterial therapy may have led to the emergence of resistant strains.

3. Reinfection with organisms different from those originally present may occur. Reinfection occurs mostly in hospital, instrumentation and catheterization being the major factors.

In a recent survey of the condition of 32 patients who had had a urinary tract infection in infancy or early childhood and who were investigated six or seven years later, Macaulay and Sutton (1957) found that five had died and were found to have gross organic deformity of the renal tract, 13 were apparently normal and 13 had either recurrent or persistent signs of urinary infection.

Summary.

Urinary tract infection has been considered under two headings—(*a*) laboratory diagnosis and (*b*) treatment.

The need for careful laboratory investigation in both diagnosis and prognosis of urinary tract infections is stressed.

Treatment has been discussed in regard to the emergence of antibiotic-resistant strains of organisms.

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British Medical Association.

VICTORIAN BRANCH: SCIENTIFIC.

A MEETING of the Victorian Branch of the British Medical Association was held on June 28, 1958, at the Bendigo and Northern Districts Base Hospital. The meeting took the form of a series of clinical demonstrations by members of the honorary medical staff of the hospital.

Volvulus of the Sigmoid Colon.

MR. A. L. NEWSON (Bendigo) showed a male patient, aged 53 years, who had been admitted to the hospital on January 17, 1958, suffering from abdominal pain and constipation. His abdomen was grossly distended. He gave a history of previous similar attacks over the past 14 years. Laparotomy was performed, and a volvulus of the sigmoid colon was reduced. The sigmoid colon was grossly elongated, dilated and hypertrophied, and full of fæces. It was abnormally long. On January 29, resection of two and a half feet of sigmoid colon was undertaken, and an end-to-end anastomosis was performed. On February 8, the patient was discharged home. Mr. Newson said that common causes of acute intestinal obstruction were (i) adhesions and bands, (ii) internal herniæ, (iii) carcinoma of the colon, (iv) intussusception. Volvulus of the sigmoid was uncommon, and hence was not often diagnosed before operation. It might be strongly suspected if there was a long history of previous milder attacks with gross abdominal distension. The best treatment was by reduction, followed by emptying of the colon with enemata, and then intraperitoneal resection. If the sigmoid was gangrenous, Mikulicz's operation should be performed.

MR. T. ACKLAND (Melbourne) said that such cases were treacherous. If nothing more was done than to return the bowel to the abdominal cavity, recurrence was possible, and it was wise to anchor the sigmoid with sutures.

DR. I. J. GORDON (Mildura) said that volvulus was common in mental hospitals, and also in the Latvian States.

Liver Suppuration: A Case for Diagnosis.

Mr. Newson then showed a male patient, aged 66 years, who had been first examined on March 18, 1958, when he complained of shivering, sweating, breathlessness, epigastric pain, anorexia and loss of weight. He was vague about the onset, but said that he had been off colour for two or three months. His bowels had been costive all his life, and there had been no recent change. He had always been healthy. A recent X-ray examination with a barium meal and a barium enema had given negative results. On examination, the patient was anæmic and cachectic. His temperature was 104° F. His liver was enlarged four inches below the costal margin and was very tender. He was admitted to hospital, and a number of investigations were undertaken over the next few days. The Casoni test produced a negative result. Examination of the chest and liver area revealed that the lungs were clear and there was no elevation of the diaphragm. No calcification was seen in the liver, but the liver seemed to be considerably enlarged. The radiologist suggested a radiological examination of the pelvis and the lumbar part of the spine. A blood count gave the following results: the hæmoglobin value was 55%, the erythrocytes numbered 3,500,000 per cubic millimetre, and the leucocytes numbered 18,000 per cubic millimetre; of the leucocytes, 200 were eosinophils. The patient's blood was of group O, and Rh-positive. In the urine a few spermatozoa were seen, as well as a few erythrocytes and pus cells. Waxy epithelial and granular casts were moderately numerous. Culture produced no growth of microorganisms. The blood failed to react to the direct Van den Bergh test. The serum bilirubin content was not increased. An X-ray examination of the lumbar part of the spine and the pelvis revealed what were considered to be secondary deposits in that area. The suggestion was Paget's disease. The appearances were most pronounced in the fourth lumbar vertebræ, and suggestive of a "vertebra nigra", such as occurred in Paget's disease. Rectal examination revealed a normal prostate. Investigation of the serum electrolytes gave the following results: the serum inorganic phosphatase level was six milligrammes per 100 millilitres, the serum acid phosphatase level was one unit, and the serum alkaline phosphatase level was 20 units. A further blood count five days after the first revealed that the erythrocytes numbered 2,600,000 per cubic millimetre, the leucocytes numbered 13,000 per cubic millimetre, and the hæmoglobin value was now 50%. On the next day, examination of a blood film revealed polymorphonuclear leucocytosis.

No definite dyscrasia was noted. On the next day, a culture of the blood yielded a growth of *Streptococcus viridans* sensitive to penicillin, streptomycin, "Chloromycetin", "Aureomycin", "Terramycin", erythromycin, tetracycline and sulphafurazole. Two days later again, the hæmoglobin value was 70%. Microscopic examination of the urine revealed a few hyaline and granular casts, pus cells and erythrocytes. Culture yielded a growth of *Staphylococcus albus*. During that time the patient remained ill, with abdominal pain, anorexia and high fever. Blood transfusions were given on March 27 and 29.

On March 30, laparotomy was undertaken, under nitrous oxide anæsthesia with a relaxant. A large abscess was found bulging out of the inferior surface of the left lobe of the liver; approximately 10 ounces of thick, creamy, odouriess pus were evacuated. The abscess wall was soft, and it looked recent. The whole of the liver was soft and engorged, with flakes of fibrin on its surface, and filmy adhesions to the diaphragm. The stomach and gall-bladder were inflamed by contiguity. The caecum was distended, but the remainder of the colon looked normal. Only limited examination of the lower part of the abdomen was carried out, for obvious reasons. Culture of pus from the liver abscess yielded a hæmolytic streptococcus. After the operation, the patient was given penicillin intramuscularly, and then erythromycin by mouth. He became afebrile after the operation, but remained weak and apathetic, and did not regain his appetite. On April 8, a blood examination gave the following results: the hæmoglobin value was 70%, the erythrocytes numbered 4,300,000 per cubic millimetre, the leucocytes numbered 8000 per cubic millimetre, and the blood urea content was 38 milligrammes per 100 millilitres. On April 10, the Kline test produced a negative result. On several occasions the stools were examined for cysts of *Entamœba histolytica*, but always with negative results. However, the patient was given a course of chloroquine and emetine injections, but without result. On April 28, he developed severe colicky lower abdominal pain, with inability to pass flatus. Rectal examination revealed tenderness high up through the anterior rectal wall, and some induration. A plain X-ray film of the abdomen revealed no evidence of large-bowel obstruction. A sigmoidoscope examination showed the rectum and the recto-sigmoid junction to be clear, but the patient could not tolerate the instrument beyond 15 centimetres.

On May 3 he was discharged home. The abdominal pain had subsided, but he required "Agarol" for his bowels. He went to his home in Melbourne, and was next examined on June 22, when he was complaining of lower abdominal pain, difficulty with his bowels and œdema of his feet. He had gained 12 pounds in weight since his last examination. His abdomen was now slightly distended, and vague lower abdominal tenderness was present. Rectal examination revealed a tender mass through the anterior rectal wall; it felt inflammatory rather than malignant. He was readmitted to hospital. On June 27, X-ray examination with a barium enema revealed that a short length of the sigmoid colon was considerably narrowed. The appearances were very suggestive of carcinoma of the sigmoid.

Mr. Newson said that liver suppuration, although it could be due to many causes, was not common, certainly not at the present time, when hydatid disease was much rarer than before. The cause in the case under discussion was thought to be portal pyæmia from infection around a lesion of the sigmoid colon, either diverticulitis or a carcinoma. If so, it would be a rare mode of presentation of either of those lesions. Chronic diverticulitis of the colon might produce inflammatory fibrosis of the bowel wall, causing almost complete stenosis. The patient had typical clinical findings of intermittent partial obstruction of the large bowel, and X-ray examination with a barium enema confirmed it. The question then arose whether the obstruction was malignant or inflammatory. It might be as difficult to determine the nature of the disease at laparotomy as before the abdomen was opened. The history, clinical findings and X-ray studies might help. A patient with chronic diverticulitis had a longer history than one with carcinoma of the colon, and the symptoms might be vaguer. Obstruction might develop more rapidly after the onset of symptoms in colonic malignant disease than in chronic diverticulitis. The passage of gross blood *per rectum* was more common in malignant disease. In chronic diverticulitis, there were more likely to be episodes of active inflammation, with signs of peritoneal irritation, such as localized pain, tenderness and perhaps a mass. The characteristic finding in the barium enema X-ray examination was obstruction due to chronic diverticulitis in a long filling defect. In the case under discussion, laparotomy was urgently necessary.

DR. W. T. C. STRAEDE (Bendigo) said that he had examined the patient six months earlier, when he had presented with abdominal pain and severe secondary anæmia. Radiological examination with a barium meal and a barium enema and sigmoidoscope examination gave negative results. Improvement had followed treatment of the patient's anæmia, and subsequently he (Dr. Straede) had heard that the patient had developed a liver abscess.

MR. NEIL JOHNSON (Melbourne) said that patients with diverticulitis and hæmorrhage could become severely anæmic, and in some cases colostomy was essential before operation on the affected area became possible.

Unusual Tumour of the Leg.

Mr. Newson's next patient was a woman, aged 70 years, who had a tumour on the medial side of her left ankle, which had been present for 28 years. The tumour was a semi-fluctuant swelling behind the medial malleolus, about five inches by four inches in area. X-ray examination revealed a little calcification in the tumour, but no bony changes. On March 20, 1958, the tumour was excised. It was encapsulated beneath deep fascia, extending behind the posterior tibial vessels and back of the tibia. Its only firm attachments were to the posterior tibial nerve, which disappeared into the capsule at the proximal pole of the tumour and reappeared at the distal pole. The nerve was sacrificed with the tumour.

Mr. Ackland said that such tumours on large nerves were very dangerous; they tended to recur, and to recur proximally in the same nerve, the recurrences becoming more and more sarcomatous. He knew of nothing which would prevent that from happening, and radiotherapy was of no value.

PROFESSOR E. S. J. KING (Melbourne) suggested that the tumour was either a neurofibroma or a leiomyoma. Its gross anatomical relation suggested the former. Solitary neurofibromata were held by Professor R. A. Willis to be not uncommon tumours, chiefly affecting young people.

Mr. Newson said that at present there was little disability from the loss of the posterior tibial nerve, which supplied the small muscles of the foot and the skin of the sole.

Subarachnoid Hæmorrhage with Hypertension and Pyelonephrosis.

Mr. Newson finally showed a female patient, aged 53 years, who in September, 1957, had had the sudden onset of very severe occipital headache and vomiting. She had suffered from thirst and polyuria for the previous two weeks. She had given a history of "kidney trouble" with each of her three pregnancies; otherwise she had always been healthy. On examination of the patient, her temperature was 99° F., her pulse rate was 120 per minute, and her blood pressure was 220/140 millimetres of mercury. Slight neck stiffness was present, and Kernig's sign was elicited. Examination of the urine revealed albumin, numerous erythrocytes, pus cells and motile bacilli. The blood urea content was 37 milligrammes per 100 millilitres. The patient's headache subsided within a day or so, but she was confused and restless at night, and had a slight irregular elevation of temperature. Slight neck and spine rigidity persisted. Further investigations were carried out. A lumbar puncture produced cerebro-spinal fluid under a pressure of 160 millimetres. The fluid was yellowish, and contained 20 cells per cubic millimetre, mainly lymphocytes. The protein content was 120 milligrammes per 100 millilitres. An X-ray examination of the chest revealed no abnormality. An intravenous pyelogram showed a normal left kidney, but the right kidney was not functioning and contained calcified masses. Culture of the urine produced a growth of coliform bacilli. *Mycobacterium tuberculosis* was not detected. On October 25 the patient was discharged home. It was concluded that she had a subarachnoid hæmorrhage, possibly associated with hypertension due to unilateral renal disease.

The patient remained well, but had a slight rise of temperature. Her urine contained albumin and pus, and her blood pressure was usually about 230/140 millimetres of mercury.

On January 16, 1958, a cystoscopic examination revealed that the bladder was normal, apart from œdema of the trigone below the right ureteric orifice. Both ureters were catheterized, and no obstruction was encountered. A dye test revealed no excretion of dye from the right kidney; it appeared from the left ureteric catheter in ten minutes. A retrograde pyelogram showed the left kidney to be normal. Calcified masses in the right kidney prevented sodium iodide from entering it.

On May 12, 1958, right nephrectomy and partial ureterectomy were performed. The right kidney was found to be

hydronephrotic and distended with turbid urine and masses of gravel and stone. There was severe fibro-fatty infiltration around the pelvis and the calyces, and the ureter was distended with turbid urine. Examination of sections revealed chronic pyelonephritis, but no evidence of tuberculosis. On May 25, the patient was discharged home. She had remained well and afebrile, but her blood pressure was still high.

Mr. Newson said that in that case a mild subarachnoid hæmorrhage was thought to be due to hypertension, which was possibly associated with unilateral renal disease. Ischæmia of the renal parenchyma led to the formation of a vasopressor substance. It was hoped that nephrectomy would lead to permanent lowering of the blood pressure.

DR. A. B. ALDER (Melbourne) said that if in patients with hypertension, who had unilateral renal disease and were subjected to nephrectomy, the blood pressure did not drop immediately, it would not drop later.

DR. ROBERT SOUTHBY (Melbourne) said that success or failure in such cases depended on how long the process had continued.

Dr. Johnson referred to the case of a girl, aged 14 years, whose blood pressure was 220/140 millimetres of mercury, and who had been investigated under Professor S. H. Lovell. During the manipulation of her damaged kidney, blood pressure rose rapidly, but after its removal it fell rapidly. Dr. Johnson agreed with Dr. Southby that if hypertension had persisted for some time, the results of nephrectomy were not good.

Intussusception Complicated by Otitic Hydrocephalus.

MR. H. M. PANNIFEX (Bendigo) showed a male infant, aged nine months, who had been first examined on the evening of September 22, 1957, having been suffering from vomiting and diarrhœa for the past five days. He had had five bowel actions that day and had vomited many times. On examination, the infant was restless and apathetic. He appeared grossly dehydrated, with sunken eyes and fontanelle and lax, dry skin. The abdomen was scaphoid and soft. No tumour was felt, numerous bowel sounds were present. His temperature was subnormal and his pulse rate was 140 per minute. It was concluded that the child was suffering from gastroenteritis. He was admitted to hospital, and intravenous therapy was begun with normal saline. Five hours after his admission, when the child had been restored somewhat with fluids given intravenously, it became evident that the abdomen was now distended. No flatus had been passed since his admission to hospital, and bowel sounds were now practically absent. The child continued to vomit brownish fluid. A plain X-ray film of the abdomen showed some coils of bowel distended with gas, but no typical ladder pattern. It was clear that the infant had an intestinal obstruction.

Laparotomy was undertaken at about 6 a.m. on September 23 under "open ether" anæsthesia, and disclosed an ileo-caecal intussusception with the apex at the hepatic flexure. On reduction of the intussusception the bowel was gangrenous, and approximately six inches of the terminal portion of the ileum and the caecum were resected. The terminal portion of the ileum was anastomosed to the transverse colon in a side-to-side manner and the abdomen closed.

On the day of operation, the infant developed a rectal temperature of 104° F., and had repeated convulsions. Lumbar puncture produced normal cerebro-spinal fluid. The convulsions were controlled with intramuscular injections of phenobarbitone. The infant seemed to improve after that. Intravenous therapy was discontinued on the second post-operative day, and the infant was taking increasing quantities of feedings by mouth.

On the third post-operative day the infant had nine bowel actions. The diarrhœa continued, and in spite of increased oral intake, which was thought to be adequately replacing the fluid lost, the infant collapsed in peripheral circulatory failure. Intravenous therapy was begun with serum, saline and glucose fluids. On the seventh post-operative day, the diarrhœa subsided and intravenous therapy was discontinued.

The infant continued to be "grizzly", with a rectal temperature of 101° F. The intravenous wound in the right leg was infected, and there was a good deal of thrombophlebitis. In addition, he appeared to be teething. He had also developed bilateral otitis media and bronchitis, in spite of "Terramycin" therapy since operation.

On October 3, both ears began discharging pus. Culture of swabs from both ears and throat grew a *Staphylococcus aureus* feebly sensitive to chloramphenicol. Oral therapy was begun with 250 milligrammes of chloramphenicol every six hours.

On October 7 (the fourteenth post-operative day), the infant was noticed to have left-sided hemiparesis. Lumbar puncture resulted in normal cerebro-spinal fluid under normal pressure, and yielding no growth of microorganisms on culture.

After one week of chloramphenicol therapy, it was obvious that the infant's condition had not improved. A change was made to "Synermycin", 125 milligrammes every six hours. Further cultures had shown the *Staphylococcus* to be insensitive to all antibiotics tested, but the sensitivity to "Synermycin" was not tested. The temperature began to subside after 36 hours. However, the infant still suffered from the left-sided weakness. It was therefore decided to transfer the child to the Royal Children's Hospital, with the diagnosis of left hemiparesis due to cerebral thrombophlebitis. Further cultures from the abscess in the right leg grew *Staphylococcus aureus* sensitive only to "Novobiocin". An ear swab yielded *Proteus*, insensitive to all antibiotics.

The baby was examined by Mr. R. S. Hooper, who considered the condition to be otitic hydrocephalus.

The child's condition gradually improved. The otitis media healed slowly with "Neomycin" ear drops, and the abscess in the right leg subsided with "Novobiocin". He was discharged home on November 12. There was still some slight residual weakness on the left side, but he looked well. In March, 1958, he developed meningococcal septicæmia, which he also survived. At the time of the meeting he appeared an alert, normal child.

Dr. Southby asked whether the case was one of systemic infection followed by intussusception and otitis. He said that such cases differed from the classical straight-out intussusception.

MR. GEORGE SWINBURNE (Melbourne), in reply to a question from Mr. Ackland, said that in cases of otitic hydrocephalus, lateral sinus thrombosis spread from one or other ear, and occluded some or all of the Paccionian bodies where the cerebro-spinal fluid was absorbed. The child presented by Mr. Pannifex had not developed papilloedema because his sutures had not closed. Mr. Swinburne said that the use of anticoagulants in such cases was not without risk, and the most important matter was control of infection.

Coarctation of the Aorta.

Mr. Pannifex also showed a girl, aged four years, who had been examined in September, 1957. She complained of pains in the legs of six weeks' duration. She had no headaches, but had had some epistaxes. Examination showed her to be a healthy-looking girl. The heart appeared clinically enlarged, with a systolic murmur and thrill over the precordium. The femoral pulses were absent. The blood pressure in the arms was 140/80 millimetres of mercury, and in the legs 80/40 millimetres of mercury; very good collateral vessels were palpable in the scapular angle.

A diagnosis of coarctation of the aorta was made, and she was referred for a cardiologist's opinion. He thought that she was a little young for operation, and that it might be possible to operate on her in about a year's time.

Idiopathic Myocarditis in Infants.

DR. A. J. WALTERS (Bendigo) said that myocarditis was known to occur as a complication of infectious diseases, notably diphtheria. It had been reported as a complication of mumps, measles, influenza, poliomyelitis, pertussis and typhoid fever. Direct infection of the myocardium had been recently shown to occur as a complication of meningoencephalitis due to Coxsackie virus, and in a wide variety of other conditions such as syphilis, tuberculosis, trichinosis, tularæmia and blastomycosis. Idiopathic myocarditis arising *per se*, and not as a complication of any other condition, was generally considered to be a rarity. That that was not so was suggested by information from Dr. Howard Williams at the Royal Children's Hospital, where over 50 such cases had been diagnosed since 1949. With the aim of stimulating interest in that condition, two further cases of idiopathic myocarditis were presented. They had occurred in infants in Bendigo in 1956.

The first case presented by Dr. Walters was that of a girl, aged six months, who had been examined on October 11, 1956, because of a history of increasing shortness of breath for 36 hours, with anorexia for solid foods. She had a past history of respiratory tract infection at the age of three months, diagnosed as bronchitis and treated with sulphonamides. There was a family history of allergy. Examination showed her to be a well-nourished, rather pale, dyspnœic baby playing unconcernedly in her cot. She was afebrile,

and the respirations were regular and rapid. There was no cough. Auscultation revealed no adventitiæ. There was a rather diminished air intake throughout, but no basal crepitations were heard. The apex beat was impalpable; the rate was regular and rapid. There were no bruits. There was no detectable hepatic enlargement or splenomegaly. Her tongue was clean, and her throat and tympanic membranes were normal. The child was thought to have asthmatic bronchitis, and treated accordingly.

The mother telephoned next day to say that the child had improved. She rang again three days later, to say that during the intervening period the child had refused solid foods and was very restless at night; also for the past 16 hours, the shortness of breath had returned and was growing worse.

On examination, the child was seen to be pale and listless, with dyspnœa as before. There was an apical triple rhythm, and the liver edge was palpable two fingers' breadth below the costal margin in the right hypochondrium. There was no œdema and no venous engorgement. The apex beat was impalpable, and there were no basal crepitations in the chest. The child was admitted to an oxygen tent in the Bendigo Base Hospital, where she collapsed and died suddenly four hours later.

At autopsy, the body was that of a well-nourished female child. There was approximately one or two ounces of straw-coloured fluid in both pleural cavities, the lungs being otherwise normal. The pericardial cavity contained a small serous exudate. The heart was anatomically normal. The myocardium was dilated and showed patchy erythema with areas of pallor. Examination of sections of the myocardium revealed scattered patchy necrosis of muscle fibres, with well-marked cellular aggregations of polymorphs and macrophages.

The second case discussed by Dr. Walters was that of a female child, aged five months, who had been admitted to the Bendigo Base Hospital on January 13, 1957, with a history that 36 hours previously she had been restless and crying and had then appeared to improve until 16 hours prior to admission, when she again was restless and crying and refused her feeds. She was noticed to be slightly short of breath 12 hours before her admission to hospital. As she had been very constipated, an enema had been given, with some relief. There was no antecedent history of any respiratory tract infection, and there was nothing else relevant in the child's past history or family history.

Examination of the patient showed her to be a well-nourished baby *in extremis*, with cold cyanosed extremities and dilated pupils. The respirations numbered 46 per minute, and were rather shallow, with no crepitations, but diminished air intake throughout. The apex beat was impalpable, but epigastric pulsation was present. The apex rate was 120 per minute. The sounds were clear, there were no bruits and the rhythm was normal. Venous distension was not observed. The abdomen was distended and tympanitic, and the liver edge was palpable three fingers' breadth below the costal margin. There was no œdema and no other relevant finding.

Despite the administration of oxygen, "Neptal" given intramuscularly and dixogin given intravenously, the baby *died 20 minutes after her admission to hospital.*

At autopsy, the only findings were a rather hæmorrhagic appearance of the myocardium and enlargement of the liver to three fingers' breadth below the costal margin in the nipple line. Microscopic examination of sections of the myocardium revealed the same patchy fragmentation of muscle fibres, with marked cellular aggregations scattered throughout the myocardium.

Discussing the difficulties arising in the diagnosis of idiopathic myocarditis in infants, Dr. Walters said that firstly, the condition progressed for an appreciable time (as judged by the microscopic findings), perhaps even to sudden fatal collapse, without causing symptoms of sufficient severity to alarm the parents or the attendant physician. In 1950, Dr. K. M. Bowden had drawn attention to myocarditis as a cause of sudden unexpected collapse in apparently healthy infants. Secondly, difficulties arose in the diagnosis of congestive cardiac failure in small babies. The apex beat was impalpable in the narrow intercostal spaces of those severely dyspnœic children. The cervical veins were hidden in the short, chubby neck. Œdema occurred late and was difficult to detect. Basal crepitations were inaudible, owing to the rapidity and shallowness of the respiratory excursions. The essential point in diagnosis was to have the condition in mind in relation to every baby who presented with dyspnœa, who was afebrile and who lacked other signs of respiratory infection. Clinical confirmation of the presence of cardiac enlargement was obtained by palpation of the cardiac impulse in the epigastric region, and by detection of hepatic enlargement—often three or four fingers' breadth below the costal margin—with the liver edge low in the right iliac fossa. X-ray examination of the chest revealed gross cardiac enlargement. Electrocardiograms might show lowering of the *QRS* complex in lead I and inverted *T* waves in leads I, II and III. Occasionally paroxysmal auricular tachycardia or heart block might complicate the myocarditis.

Dr. Walters went on to say that treatment was by careful nursing in an oxygen tent, and dixogin administered intramuscularly. Other measures might include the use of diuretics and restricted salt intake. Adrenaline and ephedrine might be indicated for patients with heart block. The prognosis was poor for patients with a short history and severe circulatory failure. However, patients with severe involvement were reported to have made a complete recovery, and others had recovered with cardiac sequelæ. In conclusion, Dr. Walters emphasized that idiopathic myocarditis was more common than was usually thought, that diagnosis depended on a search for epigastric pulsation and hepatic enlargement, that treatment depended on early diagnosis, and that recovery might follow treatment directed at the cardiac lesion.

Dr. Southby said that such cases of myocarditis in infancy were a definite entity. The illness had a rapid onset, with hurried breathing, rapid pulse and epigastric pulsation. Early digitalization was essential, and a maintenance dose of digitalis should be given for six to twelve months. Dr. Walters said that Dr. Howard Williams, of the Royal Children's Hospital, Melbourne, had said that some of the patients died, some recovered completely, and others developed valve lesions and were left with damaged hearts.

Recurrent Intussusception Treated by Barium Enemata.

Dr. Walters then presented a case of recurrent intussusception, as an example of the hydrostatic method of reduction of an intussusception in an infant. The method, which was not generally accepted, was presented for discussion as the method of choice in early cases of intussusception. The patient was a male infant, aged five months, a breast-fed child of healthy parents. He had been delivered normally at full term after a healthy pregnancy. He was examined at 8 p.m. on August 25, 1957, with the history of the sudden onset of collapse two hours earlier accompanied by vomiting and pallor. Intermittent abdominal pain was evidenced by episodes of screaming and of drawing the knees up to the abdomen. For the preceding three days the child had suffered from mild diarrhœa with anorexia and occasional vomiting. On examination, he was a pale, shocked child, crying and doubling himself up at intervals. An indefinite elongated mass was palpable in the right hypochondrium, and rectal examination caused the expulsion of typical blood-stained mucus. The child was admitted to the Bendigo Base Hospital with a diagnosis of intussusception, and transferred to the X-ray department. A lubricated Foley's catheter was inserted into the rectum and filled with 30 millilitres of warm water. A warm suspension of barium was suspended two feet above the level of the fluoroscopic screening table and allowed to run into the rectum while progress was checked on the screen. The intussusception was clearly outlined in the middle of the transverse colon, and as the pressure increased was seen rapidly to reduce, after which the barium flowed freely into the terminal portion of the ileum. The child was transferred back to a warmed bed, and the improvement was dramatic. The pulse and colour improved immediately, and within half an hour he was sleeping peacefully, his abdomen being soft and relaxed. A charcoal biscuit given by mouth was passed four hours later. The motions returned to normal, and the child was discharged home in 48 hours, feeding normally from the breast.

Progress was uneventful until September 16, when, after two days of mild diarrhœa, the intussusception recurred with similar symptomatology, and again a mass was palpable in the transverse colon. Six hours after onset, reduction was effected by the same technique, with uneventful recovery. The baby's subsequent progress was satisfactory, except that under the stress of events the mother's lactation failed and the baby was graded on to evaporated milk. At the time of the meeting he was 15 months old, and had remained free from bowel trouble.

Dr. Walters said that the case provided three points for discussion. The first was the recurrence of the intussusception. That was a recognized complication of any form of treatment. It was reported as occurring from 30 hours up

to five years after reduction. Gross's textbook, "Surgery of Infancy and Childhood", gave a recurrence rate of approximately 2%, and quoted a case in which an intussusception recurred four times in one subject. In view of the difficulty of evaluating events in the abdomen after operation, hydrostatic reduction offered obvious advantages in that respect. The second point of interest was the method used. Hipsley, in 1926, had reported a series of 100 cases of intussusception treated by hydrostatic pressure. It was only with the introduction, by such workers as Ravitch and Nordentoft, of fluoroscopic control of the procedure with a barium suspension, that the method merited consideration as a routine within the first 24 hours of onset. The two main disadvantages of the method were uncertainty as to complete reduction, and reduction or rupture of gangrenous intestine. Uncertainty about complete reduction was minimized by visual control of reduction, and by seeing the barium flow into the ileum. Reduction was confirmed by the clinical improvement and by the passage of charcoal given by mouth. Reduction or rupture of gangrenous intestine was avoided if the method was used in early cases, and the height of suspension of the enema was limited to two feet. Local exciting causes were overlooked by that method; but rarely were ileal polypi or Meckel's diverticula the cause of intussusception in infants. The implications of exposure to radiation were borne in mind, and exposure was kept to a minimium throughout the procedure. Dr. Walters suggested that the disadvantages were more than outweighed by the advantages of avoiding the hazards of anæsthesia and laparotomy in a young child.

The third point of interest was the subsequent management. The recurrence rate after non-operative reduction was said to be about five times greater than after operative reduction. Dr. Walters said that if intussusception recurred in the child under discussion, operative reduction would be indicated. He understood that if no other exciting cause was found, resection of the ileo-caecal valve would be effective in preventing recurrence. In conclusion, he said that in his opinion, hydrostatic reduction by barium enema, under visual control, was the treatment of choice in early cases of intussusception in infants.

Dr. Southby said that quite a number of patients were treated with barium enemata at the Royal Children's Hospital, but if there was a recurrence of the condition, operation was indicated.

Radiculitis.

DR. W. ROSENTHAL showed a man, aged 34 years, who was employed as a motor-truck driver when first examined in August, 1956. At that time he complained of pain in the left arm, which had commenced suddenly ten days previously. The pain radiated into the left thumb and index finger, and he noticed that the left thumb was numb. There was loss of power in the left hand. Two weeks previously he had suffered an illness of an influenzal type, had had a cough and stuffy head, and had been off work for four days. In 1952 he had suffered an aching pain in the left shoulder, which passed off quickly and was diagnosed as fibrositis.

On examination of the patient in September, 1956, there was considerable wasting and weakness of the left upper limb affecting the deltoid, the biceps (quite severely), the triceps and the extensors of the wrist and fingers, and also the small muscles of the hand. There was some weakness also of the right triceps. All the tendon reflexes in the left upper limb were reduced, and the right triceps jerk was absent. Sensory changes consisted of a loss of sensation over the left thumb and index finger extending up the radial border of the hand and forearm. Investigations of the blood and cerebro-spinal fluid failed to reveal any abnormality. The blood gave a negative reaction to the Wassermann test. The cerebro-spinal fluid pressure was normal and the fluid was clear; one lymphocyte per cubic millimetre was present. The Pandy test gave a weakly positive reaction, and the total protein content was about 25 milligrammes per 100 millilitres. The cerebro-spinal fluid gave a negative reaction to the Wassermann test.

For a period of approximately eight weeks from the onset, the nerve reactions and the voluntary movements degenerated progressively despite exercises and stimulation, until he had reached a stage at which his triceps and biceps could be stimulated only with galvanic current, and the intrinsic muscles of the hand were likewise affected. However, from that time slow progress was made with the aid of physiotherapy in the form of electrical stimulation, exercises and night splinting of his "dropped" wrist; but no worthwhile improvement was noted in the first 12 months of treatment.

In April, 1958, one year and eight months after the commencement of the illness, evaluation of the muscle strength in the left upper limb revealed an almost complete return of function, with the exception of some weakness in the extensors of the wrist and in the intrinsic muscles of the hand. Further recovery had been apparent in those muscles since that date. The sensory loss along the radial border of the forearm and about the thumb had almost completely recovered. In February, 1958, he noticed an aching pain in the right arm, and two to three weeks later wasting and loss of power of abduction became apparent, the main incidence falling on the posterior fibres of the deltoid. A muscle test in April revealed a reasonably brisk reaction to faradic stimulation of the anterior fibres of the deltoid, a weak response of the middle deltoid, and no response of the posterior fibres but a good galvanic response. A small area of impaired sensation was apparent on the outer side of the right arm. X-ray films of the cervical part of the spine were taken in August, 1956, and again in May, 1958, and no abnormality was detected on either occasion.

Dr. Rosenthal suggested that the case was one of radiculitis affecting the brachial plexus. In the first attack the fifth, sixth, seventh and eighth cervical and the first thoracic nerve roots on the left side were involved, whilst in the second attack the fifth and sixth nerve roots were the one involved. The case was considered unusual in two respects: (i) the long period of recovery of the muscles of the left upper limb—nearly two years; (ii) the recurrence of the condition involving the opposite shoulder girdle.

DR. FRANK MAY (Melbourne) said that in such cases a long recovery period was common, and electrical testing showed evidence of recovery before it was clinically detectable.

DR. M. KELLY (Melbourne) said that although in about 50% of such cases there was no apparent cause for the condition, not infrequently there was a precipitating event such as infection or an antitetanic injection.

Non-Rotation of the Gut.

Dr. Rosenthal then showed a man with congenital "non-rotation" of the gut. The patient was a metal machinist, aged 48 years. He had been first examined in March, 1958, with the complaint of prolapsing hæmorrhoids, which frequently bled and had been present for many years. His appetite was poor, and he had no energy. Chronic constipation had been present for as long as he could remember, and he regularly took large quantities of purgatives. A bilateral inguinal hernia had been present for four years, and was controlled by a truss. In April, 1958, hæmorrhoidectomy had been performed with a good result, his anal symptoms subsided, and with attention to diet he was able to dispense with all laxatives and purgatives. However, he consistently complained of a feeling of "blocking" and filling up in the lower part of the abdomen after an apparently satisfactory daily motion.

X-ray investigations of the bowel were carried out in May and June. Study of the film made during and after administration of a barium meal and enema showed the small bowel occupying the right side of the abdomen and the colon occupying the left side. The liver, spleen and stomach were normally situated. The duodenum, instead of curving round to the duodeno-jejunal flexure, made a half loop to the right and joined the jejunum on the right side below the liver. The ileum lay in the right iliac fossa. The terminal portion of the ileum ran across the mid-line to join the caecum. The ileo-caecal junction was on the right caecal wall. The caecum lay near the left iliac fossa. The ascending colon ran upwards, and bent over into a looped or folded transverse colon. It was as though the right half of the colon had been displaced concertina-wise toward the left half, and lay more or less in front of it.

Dr. Rosenthal said that it was considered that this abnormality had arisen owing to a failure of rotation in the embryonic gut between the eighth and eleventh weeks of intrauterine life. At that time the developing gut normally returned to the abdominal cavity from the umbilical cord to assume its anatomical disposition. It was believed that there the first stage of 90° rotation had occurred, but the second stage of the full 270° rotation had not been completed, the gut returning from the umbilical cord *en masse* to take up the primitive arrangement found. The patient was presented with a view to establishing the prognosis and obtaining views as to any medical or surgical measures likely to prevent the onset of complications.

Mr. Ackland, in discussing the prognosis, suggested that nothing should be done until something had happened. When that "something" had happened, it could be dealt with as necessary.

Urticaria Pigmentosa (Xanthelasmoidea).

DR. W. T. C. STRAEDE showed an infant suffering from urticaria pigmentosa. He said that there appeared to be four types of the complaint—(i) urticarial, (ii) nodular, (iii) bullous (bullæ which became macules and papules), and (iv) the condition known as telangiectasis macularis eruptiva perstans. The disease appeared usually soon after birth, and rarely persisted beyond puberty, but the pigmentation might continue. It might be seen occasionally in adults, and might follow emotional stress, and there were at least two cases recorded in which it had followed antitetanic injections. The lesions were usually confined to the trunk (posterior aspect more than anterior), the arms and the thighs. They were *chamois*, slate or brownish coloured discrete maculo-papules, and might itch. If the lesions were rubbed vigorously, urtication was produced. Old lesions became slightly atrophic spots, but new lesions were constantly appearing. Osteoporosis was sometimes found on X-ray examination, which might be suggestive of myeloma. Histologically, the principal features was an accumulation of round and stellate mast cells packed in the upper part of the corium. The mast cells had basophilic metachromatic granules, thought to be heparin monosulphate. The pigmentation was due to an increase of pigment in the basal layers. Œdema was present throughout the dermis. There was no known treatment for the disease.

Colloid Milium (Colloid Degeneration of the Skin).

Dr. Straede then showed a female patient, aged 39 years, who had noticed yellowish spots on her forehead after sunburn during the previous summer. The lesions had increased in number, and had spread from her forehead down on to the suborbital region of her face. They were small, rounded, yellowish papules, firm in consistency, discrete and symptomless. If opened, some of them contained a small amount of gelatinous substance. Histological examination revealed hyperkeratosis and atrophy of the Malpighian layer, with large masses of homogeneous material in the upper third of the dermis surrounded by collagen bundles. Treatment had consisted of the application of quinine and menthylsalicylate cream, together with chloroquine given by mouth to decrease the light sensitivity of her skin.

Contact Dermatitis due to Face Cream.

Dr. Straede finally showed a woman, aged 66 years, who had reported with swelling of her face produced by various powders and creams. That was very distressing to her, as she was particular about her attractive appearance. She tried many different brands, and then she herself used her forearms as test sites where she developed a rash; that had brought her for treatment. Dr. Straede said that he had made patch tests with a number of different face creams and powders, "Barrier Cream" and "Unibase"; all produced positive reactions. Olive oil, zinc cream and carmine gave negative results, as also did inorganic dusts such as kaolin, rouge and zinc oxide. She was therefore given a make-up kit consisting of those ingredients, with success.

Massive Hypertrophy of the Breasts in Pregnancy.

DR. W. J. LONG showed a woman, aged 31 years, who had first consulted him in November, 1953, complaining of excessive breast development since September of that year. She had had two normal confinements, in 1947 and 1950 respectively. Both babies were girls, and both had been breast-fed for three months. Normally she wore a 36-inch brassière. In February, 1953, she became pregnant, and noticed a rapid enlargement of her breasts. Spontaneous abortion occurred at two and a half months, and by that time she required a 44-inch brassière. Although she menstruated regularly after the miscarriage until September 13, 1953, there was very little reduction in the size of her breasts. Soon after that, being pregnant, she noticed the excessive hypertrophy for which she sought advice in November.

Examination of the patient showed her to be a tall, tired-looking woman of normal proportions, except for her massive mammæ, for which she was unable to find a satisfactory support. Her breasts were firm, tense and indefinitely lumpy. The superficial veins were enlarged, and the lower parts of both breasts were cyanotic and œdematous. There were two irregularly-shaped areas of necrosis on the most dependent part of the larger breast, each ulcer measuring about four by three inches, with an average depth of a quarter of an inch.

Two weeks' bed rest improved the patient's general health; but although the breasts were softer and less painful, there was little reduction in size. A double simple mastectomy was performed, the patient made a quick recovery, and the pregnancy proceeded to term. Her chest at the nipple line now measured 32 instead of its previous 54 inches.

The right breast weighed 14 pounds and the left almost 22 pounds. Pathological examination revealed that throughout the whole area, the general structure was the same—there were numerous small groups of ducts which were quite regular in form, lying in a slightly mucoid fibrous stroma. It was quite obvious that the condition was hyperplasia from a hormonal disturbance, and there was no question at all of neoplastic development.

Dr. Long said that the condition seemed to be uncommon. Geschickter had collected 27 cases of massive hypertrophy, only two being associated with pregnancy, and Burslem and Dewhurst in 1952 had reported two cases associated with pregnancy. If the breast enlargement was so great that the breasts could no longer be comfortably supported, the treatment was surgical. The marked œdema and atrophy of the nipples and surrounding skin would usually influence the surgeon in favour of amputation, rather than plastic surgery. Because it was more the end organ than the hormonal function that was at fault, endocrine therapy was unsuccessful.

Obstructed Labour due to Vagina Duplex.

Dr. Long finally showed a female patient, aged 22 years. She was a primigravida and confinement was 10 days overdue when she was admitted to the Bendigo Base Hospital on April 6, 1958. She had been admitted to hospital on the evening of April 2 and had had a dose of castor oil on the next day when the membranes ruptured. Soon afterwards she developed backache, but no satisfactory labour pains followed. The backache was constant and became more severe, but a quarter of a grain of morphine gave her a comfortable rest on each of the following nights.

By April 6 the back pain had become constant and severe. The liquor had become odorous and was almost pure meconium. The uterus was firm, but not contracting as in normal labour. The fœtal heart was not heard properly, and the mother's condition was deteriorating. Dr. Long said that when he first examined her, her temperature was 99·4° F., her pulse rate was 146 per minute, and her systolic blood pressure had risen to 190 millimetres of mercury. A catheter specimen of urine contained albumin, almost "solid" on being boiled. The uterus was firmly moulded around the fœtus, though not in a state of tonic contraction. The fœtal heart was best heard fairly low on the right side, and its rate was about 170 per minute. Pelvic examination revealed a vaginal septum, about a quarter of an inch thick, which ran from the vaginal orifice up to the internal os, where it felt as if half the presenting part was occupying a cervix dilated to admit about three fingers on each side.

A diagnosis of obstructed labour was made, and a lower segment Cæsarean section was performed under nitrous oxide and oxygen anæsthesia with "Flaxedil", administered by Dr. H. C. Purton. When the uterus was opened, a small amount of dirty and odorous liquor escaped. It was seen that the fœtus was presenting by the breech with extended legs, sitting with one buttock on each side of the septum. The baby was a living male weighing eight pounds six ounces. A large quantity of thick, foul-smelling mucus was sucked from his passages, and he was given oxygen intranasally and one millilitre of weak lobeline solution. Inspection of the lower uterine segment showed the septum to be a thick band of tissue running up to the internal os, and the cervix to be equally dilated on each side. The upper uterine segment seemed to be normal. The wound was closed and the patient returned to bed in reasonably good condition. Her urine cleared and her blood pressure dropped to normal in a few days. She was given "Terramycin" for five days, and on the fourteenth day she and her baby were discharged from hospital both well.

Dr. Long said that there were several interesting features about the case. If there was any septum in the utero-vaginal area, the defect usually started at the fundus and extended downwards. Several factors made the diagnosis and course of treatment easier by the time he saw the patient. For example, the fœtal heart rate was 170 per minute and the mother's pulse rate was 146, while previously both mother and baby had had identical pulse rates at 140 per minute. Also, at the first vaginal examination, the examining fingers were separated by the septum. The septum could easily have been missed, as it was visible only when the labia minora were widely separated, and there was ample room on each side of it to accommodate both examining fingers. Dr. Long said that he hoped before the patient's next pregnancy to divide the septum, and then give her another trial of labour.

Out of the Past.

In this column will be published from time to time extracts, taken from medical journals, newspapers, official and historical records, diaries and so on, dealing with events connected with the early medical history of Australia.

VICTORIAN BRANCH OF THE B.M.A.

FROM THE ANNUAL REPORT FOR 1895.[1]

[From the *Australasian Medical Gazette, January*, 1896.]

THIS year has been the first during which members of the Branch have received the A.M.G. in addition to the B.M.J. The result has been worth the efforts made by the different branches to establish a federal journal, and the council notes with gratification the increasing influence and importance of the Association throughout Australasia. It is hoped that the incoming year will witness the inclusion of New Zealand in the new confederation. The question of the reduction of the cost of the A.M. Gazette to members of the Branch is under consideration, and, with this satisfactorily settled, additional means will be at the disposal of the Branch for the obtainment of rooms and the establishment of a library. At present the financial arrangements of the Branch have to be kept within the narrow margin of six shillings a member.

The greatly increased secretarial work of the Branch is a matter which is commended to the consideration of the incoming Council. The relations of the Branch to the parent Association, and during this last year with the sister Branch of N.S.W., entail a great deal of routine correspondence, apart from the necessary correspondence with members, and, in addition, the Branch is being repeatedly written to by other branches in different parts of the Empire desirous of various information. The Council would recommend that the Branch should authorize the appointment of a paid assistant who could undertake the merely clerical work now pertaining to the Hon. Secretary and the Hon. Treasurer.

Public Health.

NATIONAL HEALTH AND MEDICAL RESEARCH COUNCIL.

COMMITTEE ON EPIDEMIOLOGY AND INFECTIOUS DISEASE.

THE Committee of Epidemiology and Infectious Disease of the National Health and Medical Research Council met at the Commonwealth Serum Laboratories on June 12, 1959.

Those present were Professor E. Ford (Chairman), Professor H. Ward, Dr. P. L. Bazeley, Dr. C. E. Cook and the following coopted members: Dr. E. V. Keogh, Dr. H. McLorinan, Dr. S. Fazekas, Dr. E. L. French, Dr. A. A. Ferris, Dr. R. W. Greville.

The Committee received the following requests:

1. From the National Health and Medical Research Council a request for: (*a*) an explicit statement upon polyvalent influenza virus vaccines, their efficacy, the duration of immunity conferred, their freedom from side effects and their value in the control of epidemics; (*b*) advice upon the practicability of immunization against epidemic upper respiratory tract infections.

2. From the Commissioner of Public Health, Western Australia, a request for definite answers to the following questions about influenza vaccination: (*a*) the value of vaccination where the vaccine has been prepared from the specific strain involved; (*b*) the value of a stock vaccine which contains the type but not the specific strain; (*c*) the value of a stock vaccine which does not contain the type; (*d*) time taken to develop immunity after vaccination and duration of immunity.

The following answers of the Committee are published with the approval of the Chairman of the National Health and Medical Research Council, Dr. A. J. Metcalfe.

1(a). Polyvalent Influenza Vaccine.

Efficacy. Polyvalent vaccines can afford considerable protection against the clinical effects of infection with influenza virus when the virus concerned is included in *sufficient amount* in the vaccine. Under these conditions, substantial protection (up to 75%) from clinical influenza can be expected. If, however, a new subtype of virus appears and becomes prevalent in epidemic form, no protection can be anticipated from a vaccine which does not include it. The emergence of new subtypes of virus cannot be precisely forecast, but in past experiences, new variants of influenza A have been identified at intervals of 10 to 15 years—in 1918, 1933, 1946 and 1956. With influenza B, changes have been less frequent.

Duration of Immunity. Some degree of protection may be anticipated 14 days after the administration of an adequate dose of the vaccine and maximum protection at about the second month. Protection may be expected to last from one to two years. A recommended course consists of two doses of vaccine, one month apart, followed by a reinforcing dose after an interval of 12 months.

Side Effects. At present influenza virus for use in vaccines is grown in eggs, and allergic reactions may be expected in persons sensitive to egg protein. Toxic reactions (3% to 4% general and 3% to 4% local) are likely to occur in some 6% of cases when the vaccine is given subcutaneously. If the vaccine is administered intradermally, this risk is appreciably reduced. Although theoretically the repeated injection of the egg protein content in the vaccine could produce sensitivity, this has not been observed in practice in extensive trials. It is expected that influenza vaccine from which the egg antigen has been removed will ultimately be produced.

Control of Epidemics. Although a suitable vaccine will avert the development of symptoms of clinical influenza, it cannot be expected to prevent the spread of virus through the community. It is unlikely therefore that non-vaccinated persons will be safeguarded by the protection of the vaccinated. In an epidemic year when the prevailing virus is without major antigenic change from the previous year, vaccines would be useful to protect those previously unvaccinated and those who have not experienced infection with the prevalent strain. If no new subtype appears, the vaccine should to this extent reduce the prevalence of clinical influenza. If a new antigenic subtype should appear and become epidemic, there would be little opportunity with methods at present in use to prepare, issue and administer an effective vaccine in sufficient quantity to influence the course of an epidemic.

1(b). Vaccines for Upper Respiratory Tract Infections.

The Committee considers that at present there is not sufficient evidence about upper respiratory tract infections other than influenza to justify the use of vaccines in an attempt to control them. The Committee emphasizes the desirability of the Commonwealth Serum Laboratories conducting further research into the production and value of these vaccines. In particular, assessment of their value should be undertaken by submitting them to field trial.

2. Questions from Western Australia.

In its consideration of four questions from Western Australia, the Committee has substituted the word "subtype" for the word "type" throughout. With this substitution, the Committee's answers are:

(*a*) A vaccine in which at least 100 CCA of the prevalent subtype of influenza virus is included will give up to 75% protection.
(*b*) See 1.
(*c*) No value.
(*d*) Some protection will be obtained at 14 days. Maximum protection may be expected two months after administration. If a reinforcing dose is given after the lapse of a year, protection may be expected to endure for another one or two years.

3. General.

The Committee recognizes that a number of problems related to large-scale immunization against influenza still require solution and considers that the Commonwealth Serum Laboratories should be supported in research projects, including field trials of vaccines, directed to their elucidation.

The Committee emphasizes that the value of an influenza vaccine as a prophylactic at any time will depend upon its containing in adequate amount the prevalent subtype of virus. It is important therefore that the Commonwealth Serum Laboratories as manufacturers of the vaccine should at all times be aware of the prevalence of influenza viruses in different parts of Australia.

The Committee considers that this purpose might most readily be served by the free interchange of information

[1] From the original in the Mitchell Library, Sydney.

between the Commonwealth Serum Laboratories and other virus laboratories throughout Australia. To develop an adequate liaison for this purpose the Committee suggests that an early conference of interested virologists might be arranged at the Australian National University.

In order that the scope of inquiry may be extended, health authorities might consider practicable measures to encourage the collaboration of medical practitioners in the submission of material for study by laboratories staffed and equipped for the identification of viruses.

Medical Matters in Parliament.

HOUSE OF REPRESENTATIVES.

THE following extracts from *Hansard* relate to the proceedings in the House of Representatives on August 11, 1959. They are taken from the speech of the Treasurer, Mr. Harold Holt, in presenting the Budget for 1959-1960.

Medical Benefits.

The Government intends to negotiate with registered medical benefits funds with a view to introducing a plan for considerably higher government and fund benefits for major surgery and certain other medical services. Under this plan, benefits for many surgical services will be substantially increased. The maximum combined government and fund benefit payable for a major operation is now commonly £30. This will be increased to £60. The plan will involve an increase of a few pence per week in the contributions payable by insured persons to their medical insurance organization for the increased fund benefits to be provided.

It is proposed that the necessary legislation will be introduced during these sittings of Parliament and that the plan will apply to medical services rendered on and after 1st January, 1960.

The cost is estimated to be £475,000 in a full year and £100,000 in 1959-60.

Hospital Benefits.

Last year the Government introduced a plan to make possible under the hospital and medical insurance arrangements the payment of fund benefit in chronic and pre-existing ailment cases.

Some anomalies have developed and it is now proposed to re-define and liberalize the class of case to which this special benefit will be payable. Under the new definition, claims for payment of special fund benefits for treatment in "unrecognized" hospitals will be allowed in some cases where it is established, firstly, that the patient is suffering from a condition for which he would normally be admitted to a general public hospital and secondly, that he is actually receiving hospital treatment of a standard substantially equivalent to that which he would have received at a general public hospital. Further details of the amendment proposed will be announced when the legislation is introduced, following negotiations with the hospital insurance organizations.

Tuberculosis Allowance.

Allowances payable to single and married sufferers from tuberculosis will be increased by 7s. 6d. and 15s. per week, respectively, to £6 17s. 6d. and £11 2s. 6d. per week.

The additional cost will be £80,000 in a full year, and £60,000 in 1959-60.

Pharmaceutical Benefits.

The Government has decided to make two important changes in the system under which pharmaceutical benefits are provided for the public. These changes have become necessary through revolutionary developments arising from the discovery of new and very costly drugs. It would have been contrary to the intention of the national health scheme not to make these drugs available as benefits. However, the inevitable consequence has been that many of these expensive drugs are now widely prescribed without regard to their cost, in order to save the patient the expense of paying for other drugs which are not included in the pharmaceutical benefits scheme.

The result has been to make the tax-payer responsible for a great deal of expense, much of it perhaps difficult to justify.

The cost of general pharmaceutical benefits has risen from about £3,000,000 per annum when the scheme commenced in 1950-51 to £18,455,000 last year. The number of prescriptions has increased from 3,600,000 in the first year of the scheme to an estimated 16,000,000 this year and the cost per head of population has increased from 15s. 4d. in 1951-52 to 32s. 8d. last year. It is obviously necessary to stabilize the position.

On the one hand, therefore, it has been decided to extend considerably the list of drugs which may be prescribed under the scheme so that doctors will have a choice of extending virtually over the whole field of drugs and medicines. On the other hand, a charge of 5s. will be made for each individual prescription.

Under the new arrangements the patient's position will thus be that practically every prescription written for him by his doctor will fall within the scheme. Honorable members should not forget that at present the patient receives free those drugs which come under the scheme. Many prescriptions contain drugs which do not. Whilst he will pay 5s. per prescription for a range of drugs which are now free, he will at the same time pay no more than 5s. per prescription over a range which, in many cases, would now cost him a great deal more.

The chemist's position will be that the long-standing arrangements already existing between him and the Commonwealth for payment for live-saving drugs will be extended to a comprehensive range of medicines. The fee of 5s. for each prescription will be retained by him in part payment of the cost and the Government will pay the balance.

Most pensioners now obtain a very wide range of medicines free of charge under the pensioner medical service. Their position will not be affected by the new arrangement; in other words, the medicines they obtain will continue to be entirely free.

Adequate arrangements will be made to ensure that sufferers from diseases where a specified drug is essential for the maintenance of life—for example, diabetes—will not suffer hardship by reason of the need to renew their supplies of the drugs at too frequent intervals. In these special cases payment of a single fee of 5s. will cover supplies of the drug for a reasonable period.

The full details of this plan will be announced after the Government has conferred with the professional bodies concerned, and will be the subject of legislation to be introduced later in this session.

Life Insurance and Superannuation Payments.

Consistently with its desire to encourage thrift and personal savings the Government has decided to raise to £400 the maximum allowance for life insurance premiums, superannuation contributions and similar payments. The limit is now £300.

Aged Persons.

The Government has two proposals to afford taxation relief to aged persons.

The first is to increase the level of the age allowance for taxpayers who are residents of Australia and who are qualified by age (men 65 years and women 60 years).

The second proposal relates to deductions for medical expenses paid by a taxpayer aged 65 years or over in respect of a person (either self or spouse) who has attained the age of 65 years. I know that the fear of heavy medical expenses for some chronic illness worries many elderly people in our community at the present time. In these cases, the limitation of the deduction for medical expences to £150 per person is to be removed. The concession is limited to taxpayers and their spouses and the present limit of £150 per person will continue to apply in respect of expenditure relating to other persons.

Obituary.

ERIC LEO SUSMAN.

WE are indebted to Dr. Kempson Maddox for the following account of the career of the late Dr. Eric Leo Susman.

The ability to distribute laughter is a gift beyond price. Eric Susman had this rare quality at an early age, and brightened the face and spirit of any company in which he found himself. People would begin to smile even on seeing him approach at a distance. This happy faculty

reposed not only in his sharp wit, his many well-worn clichés and his brilliant ability to sum up a man or a situation in one devastating phrase, but in his dress, his mannerisms and his affectations. He understood the temperament, the reactions, the hopes and fears of his friends and associates with an uncanny accuracy. His shafts never hurt; his criticism never wounded; his affection, kindness and loyalty were always beyond doubt. He loved people, especially young people, and no new doctor ever joined the staff of his hospital without meeting the warmth of his hospitality. He loved children, as the parents of his godchildren can testify. He made friends in all walks of life, and his abiding generosity included many acts of kindness unknown to anyone else. He had no worldly goods or pleasures which he did not share with others. He enjoyed gracious and leisurely living, rather than the synthetic and spurious diversions of an electronic age. He enjoyed games, either as a spectator—a test-match—or playing cards, where success did not follow blind chance, but required a battle of psychology with the opposition.

His schooldays at Sydney Church of England Grammar School at an end, he enlisted under age as a private in the Great War. A wound at Gallipoli brought him home to enter the Faculty of Arts at the University of Sydney, from which he soon transferred to the Faculty of Medicine, whence he graduated in 1921. Of his student days at Sydney Hospital, his residency there and at the Royal Prince Alfred Hospital and his arrival in London, there are dozens of anecdotes which have been retold amid gales of laughter. In London it was natural that he should become fascinated by the leaders of the great British School of Neurology, and by the metaphysical exercises in which the medical Colossi of the National Hospital for Nervous Diseases, Queen Square—Walshe, Holmes, Collier and Wilson—were then engaged. He could be seen striding along Piccadilly in a felt hat with a broader brim than ever seen at the Royal Easter Show in Sydney, in contrast to the narrow bowler hat, striped trousers and yellow gloves which graced Macquarie Street two years later. He was admitted as a Member of the Royal College of Physicians of London in 1924. Then followed his days of practice in King's Cross, "Locarno", the artillery hair cut and the cavalry moustache, and his appointment in 1926 as honorary physician to the Royal Prince Alfred Hospital. The rather dreary out-patient department became transformed into a happy meeting ground and the scene of many hilarious incidents, by no means all rehearsed. Between the wars he lived energetically, full of assurance and zest for life. He became a first-class cook and connoisseur of wines, *"un vrai bon viveur"*.

At the outbreak of World War II, he was called up by the Royal Australian Navy, and those of us who were fortunate enough to become his shipmates enjoyed his good company at a time when we needed it most. He kept the wardroom happy, and was loved by the ratings. During his periods of leave, which he seemed able to arrange more frequently than the rest of us, his quaint appearance in the uniform of a surgeon commander with a long brown beard, edged with white, and his little brown suitcase containing his cutlery, almost became a civic byword. After the war, he settled down to the serious business of being a senior physician, and his unique gifts as a teacher and his reputation as a "character" endeared him to his classes. Towards the end of the war, while the Johns Hopkins Unit was still with us, he organized and conducted Sunday morning medical rounds, which had quite an international character, and which formed the beginnings of the post-graduate school in medicine which distinguishes the Royal Prince Alfred Hospital at the present time. He was a "P.A." man always, and his remarkable capacity for organization, his originality and his diplomacy resulted in the squash courts, the idea of a superlatively good library, the address of welcome to new students and, just recently, the "sculpting" of the chairman of his hospital. As chairman of the Medical Board for three years, he was energetic, constructive and imaginative. In company with Campbell and Noad, Eric Susman brought back to Sydney, and maintained, the high standard of medical neurology which he had acquired in London, and instituted neurological clinics at the Royal Alexandra Hospital for Children and at his own hospital, and became the honorary director of the Northcott Clinic on the north side of the harbour. His lectures and medical papers were always most carefully prepared, memorable in their flourish and originality. Susman was a great *littérateur* in his own right. His letters and essays must be preserved. His heroes were Shakespeare, Johnson and Pepys. He was a conscientious and consistent diarist, and extremely punctilious in his correspondence and business affairs. In addition, he had a keen and penetrating appreciation of art, music, sculpture and the theatre. The Susman Art Prize at the Sydney Technical College was established many years ago, and Fred Leist and A. Mezaros were his close friends.

In spite of a superficial flamboyancy and a tempestuous life, Eric Susman was a sensitive, modest man, never a snob, a good son and a loyal friend, and with a capacity for sharing confidences which his women friends perhaps would appreciate more than his men friends. He was a man of contrasts, shrewd and careful; a generous, devastating critic, but prepared to receive in good temper as much as he gave; unconventional, but with a strong sense of tradition and timing; apparently untidy, but obsessionally systematic. He had exceptional business and organizing ability, and would have succeeded in many fields of life other than medicine. *Bon viveur*, brilliant

satirist, gifted speaker, constant friend, he had something in him of Byron, Edward VII and Alexander Woollcott. He was a great Australian, a distinguished son of his hospital and city, and it was our great good fortune and privilege to be his contemporaries. We shall finish and maintain the many things he has achieved in his colourful career.

Eric Susman was a man of great courage, and only a few would guess the depth of his physical suffering over the years. The vivid personality at the moment is too close for us to realize fully the jagged hole which his passing will leave in our lives. Our own remaining days are suddenly bereft of much sunshine and laughter.

DR. NICHOLAS LARKINS writes: The untimely death of Eric Susman has created a great void. He was one of the most colourful and unique characters that the profession of medicine in Sydney has produced. The majority of his professional life was concerned with teaching, both post-graduate and undergraduate, at his beloved "Prince Alfred". He assessed himself as an exhibitionistic extrovert, and his *modus operandi* was his flair for the rococo and bizarre applied both to behaviour and to his method of expression. He was a master of English and adored the use of the paradox, the double negative, the less common synonyms for well-known places, a deliberate and mischievous mispronunciation of proper names. "There will be many a dry eye when he passes Pinchgut outward bound", he said of an unpopular character based on Sydney during the war. This capacity gave him tremendous power as a lecturer, teacher, writer and conversationalist, for he was

outstanding as all of these. He had a diversity of interests. An avid reader, a lover of the fine arts, of music and the art of living, he was an authority on wine and food and a superb host. He had tremendous drive and application for work, a fantastic gift for interesting himself in all acquaintances, and to his closer friends he was devoted. And his friends are in every walk of life and of all ages—from Scot Skirving to the school children (particularly those of his friends), from admirals to ordinary seamen, from painters to cartoonists, from judges to articled clerks. Susman found it effortless to remain streamlined in mind and attitude and interests, and yet he paradoxically ignored many new things. Except for the briefest interval (when he employed a female driver) he owned no car, could not drive and pretended "an incapacity to cope with the vagaries of the internal combustion engine". He was, nevertheless, essentially practical and realistic, and reacted with forceful invective on any subject or person which offended his sense of adequacy. Of a late knighthood conferred on a distinguished member of the profession, he said: "What is the use of knighting a man who is little more than a puff of smoke from a crematorium chimney?"

By his death at the age of 63, the profession has lost, as well also his friends, a most fascinating associate who served in two World Wars and was outstanding in his profession as a teacher and practitioner, as well as an outstanding character and personality. To transpose "Susmania", "There is many a wet eye as he passes outward bound", in his Puckish way no doubt to reorganize and add colour to the hereafter.

DR. RAYMOND HENNESSY writes: Dr. Samuel Johnson said of his friend Edmund Burke: "Yes, sir, if a man were to come by chance at the same time with Burke under a shed to shun a shower he would say 'This is an extraordinary man.' If Burke should go into a stable to see his horse drest the ostler would say 'We have an extraordinary man here.'" Most people acquainted with him would agree that these remarks fairly apply also to the late Eric Susman. He was above all else an original and vigorous personality. I vividly recall our first meeting—it was in July, 1923, at a London hospital. Susman had just completed a term as house physician with Purves Stewart at Westminster Hospital. Susman and I were interested in the subject of Quincke's disease, the ætiology of which, at that time, was not fully elucidated. I well recall that our discussion went well into the early morning. Since then our lives have been curiously interwoven.

Susman's chief characteristics were his animated conversation, his bustling vitality and boisterous enthusiasm. Like David Garrick, he was the first man of the world for sprightly conversation. His curiosity was universal, and like Bacon, he took all knowledge for his province.

His life was full of incident and adventure. At the age of 18 years he enlisted in the First Australian Imperial Force, and was in the second landing at Gallipoli, where he remained till the evacuation. At that time he suffered severely from diabetes insipidus, and as the shortage of water on the peninsula was constant and severe, one can imagine his terrible privations above all his companions. He often said that the first thing he did when he saw a dead soldier, friend or foe, was to grab his water bag.

He was sent back to Sydney and completed his medical course, graduating in 1921. He served a term as resident medical officer at the Royal Prince Alfred Hospital. He then went to England, and obtained the diploma of Membership of the Royal College of Physicians in 1924. He was elected a Fellow of The Royal Australasian College of Physicians in 1938. By nature and by choice he was attracted to the study of neurology, and after being house physician at Westminster Hospital and West London Hospital he served a term at the National Hospital, Queen Square.

Susman commenced practice in Sydney towards the end of 1925, and in the following year was appointed to the staff of the Royal Prince Alfred Hospital—an association with the hospital which regulated his entire medical life and terminated only with his death. Between the two World Wars he joined the Royal Australian Naval Reserve, and was called up for duty in the Navy at the outbreak of war in September, 1939. He served most of the time at sea, generally in defenceless ships during the cruellest naval warfare in history. Although no man loved and used the comforts of life more, he cheerfully adapted himself to all the discomforts and dangers of shipboard life under war conditions.

Apart from his military and naval experiences, which took him practically all over the world, he made several private visits to England, Europe and the United States of America, the most recent being in 1957.

As a physician he was not deeply read in medicine. He read men's minds more readily than he read men's books, but he was a shrewd observer and learnt eagerly by viva voce. He was quick in sizing up a situation. His talents were best suited to cases of a bizarre and esoteric nature, and he loved those which had a human interest. His hands were exquisitely shaped, and he was adroit in any manipulation. For instance, he quickly became proficient in cistern puncture when it was first introduced into clinical medicine.

As a host Susman was incomparable, whether at *tête-à-tête* or a large formal gathering. He delighted in arranging and organizing to the last detail. He would inspect the food as it came into the kitchen and before it was prepared and cooked. His taste in wine was cultivated and reliable. He studied cooking seriously and was well accomplished, and loved to prepare meals for his guests in his own apartment. He was interested in all the polite arts, and was somewhat of a connoisseur in painting. He had an extraordinary gift for friendship and for convening and maintaining social groups.

All games of chance requiring the quick use of wits appealed to him, and he was superb at every kind of card game. He was not really musical, but he understood and appreciated music, which he studied as part of general culture, and he was instinctively attracted by the philosophy of the Wagnerian operas. He was an ardent theatre-goer and his tastes were amorphous, but he was particularly fond of the plays of William Shakespeare and of Bernard Shaw.

He was fond of feminine society, and few men knew better how to humour the ladies, were more assiduous to please them, or better understood their foibles. He loved to retail petty gossip, which he nothing extenuated, nor did he set down aught in malice.

He was very fond of teaching, but was not, I think, a good lecturer in the formal manner. He was rather inclined to overstate his case and overact his part. He was at his best in unpremeditated talks and discussions. His best written contribution was entitled "The Psychological Aspect of Deafness", delivered before the Australasian Medical Congress (British Medical Association) in Hobart in 1958—but this was written *con amore*. His private practice was lucrative but never very large; it merely filled the interstices of his hospital duties, which he took very seriously, and his social life, which was very full. He was always financially independent of his medical earnings. He did everything with gusto; even his personal daily routine of toilet was lavish and prolonged. He had a strong statistical instinct; for many years he kept a minute account of all his petty spendings, balancing each night even to the last halfpenny. His enthusiasm was contagious, and his vivacious narrative powers carried his listeners along with him. When he was introduced into a company of strangers, he was generally found dominating the party by the end of the evening. For many years he consistently kept a diary; his war diaries he has bequeathed to the Mitchell Library, with instructions that they are not to be examined or published until the year 2000. They should make good reading.

His health failed rapidly during the last twelve months, and he was very interested in the nature of his malady, which was a puzzle to his medical advisers. I think he knew that it was gaining on him. He ordered his body to be opened after death, and allowed a generous emolument for the pathologist. His death was instantaneous—which was the only thing his medical advisers were unanimous in agreeing would not happen to him.

I loved the man, and gladly do honour to his memory, on this side idolatry. The words of Oliver Goldsmith accurately describe him—he was an abridgement of all that is pleasant in man.

Correspondence.

THE SUSMAN LIBRARY COMMITTEE.

SIR: On the occasion of his retirement as Senior Physician of Royal Prince Alfred Hospital, Dr. Eric Susman presented to the Board the sum of £5000 for the purpose of establishing and equipping a modern clinical library. His gift was prompted by his appreciation of the vital necessity for all students of medicine to have the benefit of ready access to a complete reference library housed and managed under conditions appropriate to study. It was his dearest wish that this library, as to

its contents, its setting and its management, should rank with the finest scientific and clinical libraries in the world.

A great deal of preliminary planning was carried out by the librarians of the Fisher and Mitchell Libraries and by the Director of the Public Library. It became apparent after considering their recommendations and the cost of equipping and staffing the library, that Dr. Susman's gift was far short of the total amount which would be required to establish the library along the lines contemplated by him. It was at this stage that he persuaded his great friend, Mr. George Falkiner, to help with a contribution, but even his generosity has not bridged the gap.

It has occurred to me, and indeed has also been suggested to me by a number of Eric Susman's friends, that there are many people, both inside and outside the medical profession, who would like an opportunity of perpetuating his memory in a fitting manner, and at the same time do a great service to the medical profession. Even his non-medical friends, I am sure, are aware of the devotion with which he applied himself to his task as Warden of Clinical Studies, and of his enormous and untiring interest in the teaching and welfare of the young men in the Faculty of Medicine. Personally I feel that no memorial could be more fitting than that this library should be the success that he had wished and fulfil the high hopes that he himself had cherished. It is for that reason that we have formed a small committee to give the opportunity to his friends of sharing in its cost.

I feel there is no point in stating the maximum amount required, because whatever is received can be spent to good purpose, and if the total is of a generous nature it would permit of some portion being spent on a memorial plaque, inscribed in a manner which would do justice to his memory. It is perhaps unnecessary to point out that all donations would be deductible for income tax purposes. If you are minded to contribute, would you be good enough to forward a cheque to Royal Prince Alfred Hospital Susman Library Fund, Missenden Road, Camperdown, N.S.W.?

Yours, etc.

H. H. SCHLINK,
Chairman, Royal Prince Alfred Hospital Susman Library Fund.

Royal Prince Alfred Hospital,
Camperdown,
New South Wales.
July 20, 1959.

STEROID HORMONES: II. SEX HORMONES.

SIR: In your issue of August 8, "Brush up Your Medicine", a most interesting article appeared covering androgens and œstrogens. Table I, which listed the androgens, gave the preparation and strength of "Halotestin" as an ampoule of 25 mg.

"Halotestin" is not marketed in the ampoule form, but is available as a 5 mg. oral tablet. A small number of ampoules were prepared for certain clinical trials, but as it was quickly established that the oral therapy gave better results on a milligramme for milligramme basis, parenteral "Halotestin" has never become commercially available. Oral "Halotestin", unlike most oral testosterone derivatives, is not attacked by the enzyme systems of the liver, and reaches the general circulation in its intact form.

Yours, etc.,

F. J. COLLINGS.

The Upjohn Company (Aust.) Pty. Limited,
55-73 Kirby Street,
Rydalmere, N.S.W.
August 17, 1959.

TOBACCO SMOKING AND LUNG CANCER.

SIR: Perhaps the principal reason why medical science appears to have received such a resounding defeat in its attempt to convince society that cigarette smoking causes lung cancer is the muddled thinking of many of those who join in the discussion, and despite his well-deserved eminence in surgical matters, Mr. K. W. Starr must be classed with the muddled-thinkers on this subject. Has medical science received such a defeat? In my opinion it has not, and the defeat, if any, lies at the door of the statistical scientists, who have failed to convince more than a small proportion of medical scientists of the validity of their claims. Medical science receives, not defeat, but discredit for its failure to face up to the facts, for this failure helps to convince a lay public, only too anxious to be convinced, that what appears statistically to be incontrovertibly true is, in some way not explained, really false.

Does the community remain indifferent? In Adelaide, at least, there is a general uneasiness that, despite the failure of the medical profession to give clear advice about it, there is indeed some definite relationship between the smoking of cigarettes and cancer of the lung. The average citizen who smokes takes comfort from the "waffllings" of letters like that of Mr. Starr and from statements such as those of Sir Ronald Fisher; he does not fully believe Sir Ronald's disclaimers, but he accepts them to mean that the unpopular warnings of the scientists are not as serious as they would seem to be. There are very few parents in these days who, without misgivings, see their children starting to smoke cigarettes.

It would take a small monograph to answer all the statements, some true but many palpably false, which Mr. Starr has included in his letter to you, published on August 8. It is not true that science has used statistics to show a causal relationship. It has used the statistical method to investigate the proposition that a relationship exists between smoking and subsequent cancer of the lung, and has proved this to the degree that no unbiased person can fail to accept it; it deduces that such an association is best explained as direct cause and effect, but it does not prove this. Percy Stocks is not fairly reported, for while he blames pollution for some of the lung cancer in cities, he blames smoking for more, and he has said that if in a rural community the population were to stop smoking, cancer of the lung would become a rare disease in 25 years. It is not true that statisticians have failed to explain male dominance in lung cancer. In the United Kingdom in 1920,[1] the average male consumption of tobacco in the form of cigarettes was 5·1 lb. and the average female consumption negligible. In 1930 the respective figures are 6·1 lb. and 0·4 lb., and in 1940, 7·9 lb. and 1·3 lb. A superficial look at women smokers today may give the impression which Mr. Starr has stated, but if we assume a long latent period such as exists in cancer production by a number of known carcinogens, is not the relatively lower female lung-cancer rate just what would be expected by the statisticians without invoking sex differences in susceptibility? In 1958 men were smoking 8·3 lb. per head as against 3·3 lb. for women, and I would suggest that the sex difference in incidence will continue, even although the rate of lung-cancer incidence in women is rising.

Are non-European races immune? I know of no statistical survey in this regard, except in the United States, where I believe such an immunity has not been shown among coloured people. The higher tobacco consumption of the United States is open to question, for there is statistical evidence that the American butt is appreciably larger than the British, a fact which will surprise no-one who has stood, say, on the platform of Pennsylvania subway station in New York and seen masses of what appear to be almost whole cigarettes "used", but not "smoked"

There is very much more to be said, but we all know it. Let us not accept the implication of Mr. Starr's last paragraph, that because other cancers might develop if lung cancer is abolished, we should do nothing about lung cancer. Let us rather as a body say that there is some relationship between smoking and lung cancer not as yet fully understood, and take a chance that other cancers will not fill the gap which is bound to follow.

Yours, etc.,

B. S. HANSON.

163 North Terrace,
Adelaide.
August 12, 1959.

SIR: Dr. K. V. Starr's letter (MED. J. AUST., August 8), while an interesting account of his personal disbelief in the matter of the relationship of tobacco smoking and lung cancer, does nothing to help those responsible for the public health, nor is it of any assistance to the clinician whose unfortunate duty it is to diagnose and attempt to treat these cases.

His assertion that "science has based its contentions on statistics . . . in an effort to show a causal relationship" is far too superficial an appraisal of the tremendous amount of objective consideration that this problem has received to be allowed to pass without comment.

[1] Tobacco Manufacturers' Standing Committee, Research Paper, No. 1: "Statistics of Smoking", 2nd edition: 10 and 11

The fact is that statistics have shown an intimate association and that, despite much criticism, the association has, as yet, been explained in no other way at all satisfying to an unbiased observer, than by assuming a causal association. This is a far cry from proving a casual relationship.

When, however, one considers that the chance of developing cancer can be forecast in a prospective survey with considerable success, knowing only the place of residence, sex and smoking habits of a group of individuals, that stopping smoking decreases the chances of an individual contracting lung cancer, and that histologically it is only squamous-celled carcinoma which is so influenced, the case made, purely on statistics alone, is one which is extremely difficult to refute.

Moreover, when statistical evidence suggested that carcinogens might occur in tobacco tar, a search revealed their presence.

Stocks's evidence (also statistical incidentally. Why accept one man's statistical conclusion and not another's?) in no way opposes the tobacco-cancer association, but supports it, with the evidence that residence in cities, presumably due to atmospheric pollution, is an additional factor of statistical importance. The presence of known carcinogenic combustion products in both tobacco smoke and city atmosphere provides a common factor, which may explain why the hard-smoking city man has a higher lung cancer death rate than the hard-smoking country dweller.

Dr. Starr suggests that the elimination of tobacco would result in a balancing increase in cancer of a different site. Could he suggest at which site or sites the incidence is falling to a degree corresponding to the 7% per annum rise in lung cancer currently occurring in Australia?; and even if his statement is by chance correct, the transfer of the cancer from the lung to the colon would mean its transfer from a virtually untreatable to a possibly curable site—no bad thing to contemplate.

There can be no doubt that if a tenth of the statistical evidence involving tobacco was pointed at some less popular human habit—such as painting one's house with lead paint—there would be an overwhelming demand for instant Governmental action to suppress this, and to save individuals from their own folly.

In view of the tremendous vested interests of both Government and industry in tobacco, the aims of the interested have been very modest—to try and influence young people against smoking and to attempt to discover some means of removing the carcinogens from tobacco.

Percivall Pott, in 1775, disclosed the ætiology of chimney sweep's cancer, and prescribed methods for its prevention, even if the academic proof of his theory was not produced until Passey, in 1922, produced cancer in animals by soot—which may not even now be accepted as a proof by all research workers. Our forefathers with practical sense realized the truth of a recent editorial statement in the *British Medical Journal*; that all we "can do is to show that the probability of a causative connection between an agent and disease is so great that we are bound to take what preventive action we can accepting the theory as though the proof was absolute until further research leads to some modification".

To many a modern view the final proof of the ætiology of chimney sweep's cancer was produced by its prevention.

May we show the same practical sense as our forefathers, and not look for direct proofs, which are out of reach before we transmit experience into practical measures. They would indeed be hard measures which would be intolerable, could they give only a well-founded hope of diminishing the very serious endemic of pulmonary cancer ahead.[1]

Yours, etc.,
E. W. ABRAHAMS.

Chest Clinic,
81 George Street,
Brisbane.
August 14, 1959.

SIR: Dr. Kenneth W. Starr makes an ineffectual attempt to discredit the medical research worker who has established a causative link between cigarette smoking and lung cancer (MED. J. AUST., August 8, 1959). Few, if any, of your readers will agree with his statement that medical science has suffered a "most resounding defeat".

Dr. Starr has not refuted the mass of evidence supplied by Doll and Hill, of Great Britain, and by Wynder and Graham, of the United States. Furthermore, he has ignored the other diseases which may be caused or aggravated by excessive smoking. The Vice-President of the American Cancer Society stated that "the problems raised by the effects of smoking on the heart and arteries were even more pressing than were the more publicized findings linking smoking and lung cancer" (*Brit. med. J.*, January 8, 1955).

Chronic pharyngitis and chronic bronchitis are often associated with excessive smoking, while tobacco amblyopia is familiar to oculists. Smoking is the most important factor in the causation of thromboarteritis obliterans (Buerger's disease). In the *Proceedings of the Staff Meetings of the Mayo Clinic* (August 13, 1952) there is a report by four medical research workers who state that "no patient who suffers from asthma should smoke".

The education of the people in health matters is a slow process, and any statements which conflict with the best medical opinion should be most carefully considered. Every man is entitled to his opinion; but, by those of us who attach importance to preventive medicine, Dr. Starr's letter can only be regarded as irresponsible.

Yours, etc.,
VICTOR H. WALLACE.

61 Collins Street,
Melbourne.
August 11, 1959.

SIR: I was interested to read Dr. Kenneth Starr's letter (Journal, August 8) in which he quoted some figures from my talk to the Cancer Research Group at the Prince of Wales Hospital. This was a preliminary report on 170 males and 18 females with proven bronchial carcinoma detected in mass X-ray surveys in the metropolitan area of Sydney between 1953 and 1956, when a total of 1,686,454 persons were X-rayed.

A number of probable carcinomas were not included, as some patients could not be traced and others refused investigation and their diagnosis remained in doubt. I hope to publish a full report on carcinoma detection in mass X-ray surveys at a later date.

With regard to smoking, the findings in the 188 proven cases are similar to data obtained overseas; 134 were smokers, all of whom, with the exception of two, were cigarette smokers, 15 were non-smokers, 14 had previously smoked and the smoking habits of 25 remain unknown.

Analysis of occupations, place of residence and racial origin of patients in this series would indicate that these could be important factors, worthy of as much investigation as smoking habits.

In my opinion, irrespective of the various causative factors, early diagnosis of lung cancer is still of prime importance. With the current practice of mass surveys at two-yearly intervals we found that 57·4% of cases in this series were considered inoperable when detected. If early diagnosis is to be achieved, some authorities recommend six-monthly chest X-ray for men over 40.

Yours, etc.,
C. RUBINSTEIN.

Anti-Tuberculosis Association of New South Wales,
Corner of Crown and Foveaux Streets,
Surry Hills, N.S.W.
August 11, 1959.

[1] Cancer of Lung—A Symposium, *Unionis Internationalis Contra Cancrum*, Paris, 1953.

Post-Graduate Work.

THE POST-GRADUATE COMMITTEE IN MEDICINE IN THE UNIVERSITY OF SYDNEY.

Post-Graduate Conference at Young.

THE Post-Graduate Committee in Medicine in the University of Sydney announces that in conjunction with the Young Medical Group, a Post-Graduate Conference will be held in the Board Room, Young District Hospital, on Saturday and Sunday, September 19 and 20, 1959. The programme is as follows:

Saturday, September 19: 2 p.m., registration; 2.30 p.m., "Intestinal Obstruction", Dr. Alan Sharp; 4 p.m., "Management of Coronary Artery Disease", Dr. Frank L. Ritchie.

Sunday, September 20: 10 a.m., "Vascular Surgery with Particular Reference to Varicose Veins", Dr. Alan Sharp; 11.30 a.m., "Management of Hypertension", Dr. Frank L. Ritchie.

The fee for attendance at the course is £3 3s., and those wishing to attend are requested to notify Dr. James Purchas, Honorary Secretary, Young Medical Group, 12 Boorowa Street, Young, as soon as possible. Telephones: Young 304 and 403.

Post-Graduate Conference at Kempsey.

The Post-Graduate Committee in Medicine in the University of Sydney announces that in conjunction with the Eastern District Medical Association, a Post-Graduate Conference will be held at the Macleay District Hospital, Kempsey, on Saturday and Sunday, September 26 and 27, 1959. The programme is as follows:

Saturday, September 26: 2 p.m., registration; 2.30 p.m., "The Early Diagnosis of Cerebral Tumours", Dr. W. Scott Charlton; 4 p.m. to 5.30 p.m., "The Indications and Results of Surgical Treatment for Parkinson's Disease—with film", Dr. George Selby.

Sunday, September 27: 9.30 a.m., "Recent Advances in Treatment of Epilepsy", Dr. W. Scott Charlton; 11 a.m., "The Management of Cerebral Vascular Disease", Dr. George Selby; 12 noon to 1 p.m., quiz session; 2.30 p.m., Eastern District Medical Association annual meeting.

The fee for attendance at the course is £3 3s., and those wishing to attend are requested to notify Dr. H. E. Masters, Honorary Secretary, Eastern District Association, 9 Oxley Street, Taree, as soon as possible. Telephone: Taree 1212.

Grants for Research into Cancer.

Advice has been received from the Secretary, New South Wales State Cancer Council, to the effect that funds are available to the Council for further research into cancer.

Applications are now being invited for grants in respect of (*a*) research fellowships; (*b*) travelling fellowships; (*c*) grants-in-aid.

The closing date for the lodgement of applications is October 12, 1959, and such applications must reach the Secretary, New South Wales State Cancer Council, Box 3944, G.P.O., Sydney, or The Basement, Treasury Building, Bridge Street, Sydney, no later than that date.

Application forms and further details may be obtained from the Secretary at the above-mentioned address.

ROYAL PRINCE ALFRED HOSPITAL: EAR, NOSE AND THROAT DEPARTMENT.

Seminar Programme, 1959.

THE staff of the ear, nose and throat department of the Royal Prince Alfred Hospital will conduct a seminar on the second Saturday of every month at 8 a.m. in the Scot Skirving Lecture Theatre. The main speaker will not exceed forty minutes, and there will be a discussion at the conclusion of his remarks. All medical practitioners and clinical students are invited to attend.

At the next seminar, to be held on September 12, 1959. Dr. J. H. Lancken will speak on "Diverticula of the Pharynx".

THE MELBOURNE MEDICAL POST-GRADUATE COMMITTEE.

Refresher Course for General Practitioners at the Royal Melbourne Hospital.

THE Melbourne Medical Post-Graduate Committee will conduct a refresher course for general practitioners at the Royal Melbourne Hospital from September 21 to 25, 1959. The programme will be as follows:

Monday, September 21: 9 a.m. to 10.30 a.m., Dr. L. E. Rothstadt; 11 a.m. to 12.30 p.m., Mr. G. Swinburne; 2 p.m. to 3.30 p.m. (gynæcology), Mr. L. W. Gleadell; 3.45 p.m. to 5.15 p.m. (ophthalmoolgy), Dr. T. a'B. Travers.

Tuesday, September 22: 9 a.m. to 10.30 a.m., Dr. J. H. Bolton; 11 a.m. to 12.30 p.m., Mr. W. E. A. Hughes-Jones; 2 p.m. to 3 p.m. (neurology), Dr. E. G. Robertson; 3.15 p.m. to 4.15 p.m. (neurosurgery), Mr. R. S. Hooper; 4.30 p.m. to 5.15 p.m. (urology), Mr. J. B. Somerset.

Wednesday, September 23: morning, Fairfield Hospital; 2 p.m. to 3.30 p.m., Mr. J. O. Smith; 3.45 p.m. to 5.15 p.m. (orthopædics), Mr. B. T. Keon-Cohen; 7 p.m. (dermatology), Dr. I. O. Stahle; (endocrinology), Dr. H. P. Taft.

Thursday, September 24: Show Day, public holiday.

Friday, September 25: 9 a.m. to 10.30 a.m., Professor R. R. H. Lovell; 11 a.m. to 12.30 p.m., Professor M. R.

DISEASES NOTIFIED IN EACH STATE AND TERRITORY OF AUSTRALIA FOR THE WEEK ENDED AUGUST 1, 1959.[1]

Disease.	New South Wales.	Victoria.	Queensland.	South Australia.	Western Australia.	Tasmania.	Northern Territory.	Australian Capital Territory.	Australia.
Acute Rheumatism	..	2(2)	1(1)	..	..	..	..	..	3
Amœbiasis	..	..	..	..	..	..	..	..	..
Ancylostomiasis	1	..	..	..	..	..	11	..	12
Anthrax	..	..	..	..	..	..	..	..	..
Bilharziasis	..	..	..	..	..	..	..	..	..
Brucellosis	..	1	..	..	..	..	..	..	1
Cholera	..	..	..	..	..	..	..	..	..
Chorea (St. Vitus)	..	..	..	..	..	..	..	..	..
Dengue	..	..	..	..	..	..	..	..	..
Diarrhœa (Infantile)	1(1)	18(17)	2(2)	..	1(1)	..	..	1	23
Diphtheria	..	..	..	..	2(2)	..	..	..	2
Dysentery (Bacillary)	..	2(2)	1	1(1)	3(2)	..	1	..	8
Encephalitis	..	3(2)	..	..	..	..	..	..	3
Filariasis	..	..	..	..	..	..	..	..	..
Homologous Serum Jaundice	..	..	..	..	..	..	..	..	..
Hydatid	..	..	..	..	..	..	..	..	..
Infective Hepatitis	60(22)	15(7)	9(2)	4	3(2)	..	..	..	91
Lead Poisoning	..	..	..	..	..	..	..	..	..
Leprosy	..	..	..	..	..	..	1	..	1
Leptospirosis	..	..	5	..	..	..	..	..	5
Malaria	..	..	..	..	..	..	1	..	1
Meningococcal Infection	2(2)	1	1	..	..	1	1	..	6
Ophthalmia	..	..	..	..	..	..	..	1	1
Ornithosis	..	..	..	..	..	..	..	..	..
Paratyphoid	..	..	..	..	..	1	..	..	1
Plague	..	..	..	..	..	..	..	..	..
Poliomyelitis	..	2(2)	..	..	..	..	..	..	2
Puerperal Fever	1	..	..	..	..	..	..	..	1
Rubella	..	22(19)	..	2	1(1)	..	..	..	25
Salmonella Infection	..	..	..	2(1)	2(2)	..	..	..	4
Scarlet Fever	7(2)	27(21)	3(1)	4(2)	..	1	..	..	42
Smallpox	..	..	..	..	..	..	..	..	..
Tetanus	..	..	..	..	1(1)	..	..	..	1
Trachoma	..	..	..	..	..	..	5	..	5
Trichinosis	..	..	..	..	..	..	..	..	..
Tuberculosis	18(7)	22(19)	4(1)	6(4)	6(3)	3	2	..	63
Typhoid Fever	..	..	..	..	..	..	..	..	..
Typhus (Flea-, Mite- and Tick-borne)	..	..	..	..	..	..	..	..	..
Typhus (Louse-borne)	..	..	..	..	..	..	..	..	..
Yellow Fever	..	..	..	..	..	..	..	..	..

[1] Figures in parentheses are those for the metropolitan area.

Ewing; 2 p.m. to 3 p.m. (allergy), Dr. R. H. O. Donald; 3.15 p.m. to 4.15 p.m. (thoracic surgery), Mr. J. I. Hayward; 4.15 p.m. to 4.35 p.m., film entitled "Cardiac Arrest".

The fee for this course is £9, and enrolments should be made with the Melbourne Medical Post-Graduate Committee as soon as possible.

University Intelligence.

UNIVERSITY OF MELBOURNE.

Elections to Council and Standing Committee of Convocation by Graduates.

NOTICE is hereby given that nominations will be received up to 4 p.m. on Monday, September 21, 1959, to fill five vacancies for the representatives of graduates on the Council of the University of Melbourne and 22 vacancies for the representatives of graduates of all faculties on the Standing Committee of Convocation. Nomination forms may be obtained from the Returning Officer.

Notes and News.

TWO REHABILITATION MEETINGS IN BRISBANE.

THE Principal Medical Officer of the Commonwealth Department of Social Services, Central Administration, announces that two meetings are being arranged in Brisbane as part of a seminar on rehabilitation for medical officers of the Commonwealth Rehabilitation Service (Department of Social Services), which will be held from September 14 to 18, 1959.

On Wednesday, September 16, an "open day" for members of the medical profession, final-year medical students and members of relevant ancillary professions will be held at *2 p.m. at Kingshome Rehabilitation Centre, 170 Swann* Road, Taringa, Brisbane. Cases illustrating various problems of rehabilitation will be presented for discussion by *Dr. G. A. McLean, the Medical Director of the Centre, and* by sessional consultants. Afternoon tea will be served.

On Thursday, September 17, at 8.15 p.m., at the Medical *School, University of Queensland, a forum on "Cardio-*Vascular Rehabilitation" will be held, to which all interested members of the medical profession and of ancillary professions are invited. The moderator of this session will be Sir Alexander Murphy, F.R.C.P., F.R.A.C.P., and the participants in the forum will be Dr. N. V. Youngman, *F.R.A.C.P., Dr. E. G. Gales, M.R.C.P., M.R.A.C.P.*, and Dr. G. A. McLean, Senior Medical Officer, Department of Social Services, Queensland, and Medical Director of Kingshome *Rehabilitation Centre.*

Nominations and Elections.

THE undermentioned have applied for election as members of the New South Wales Branch of the British Medical Association:

Jackus, Boris, M.D., 1937 (Univ. Kaunas), (registered under Section 17 (2B)), Namatanai, New Ireland *District, New Guinea.*

Mead, Phillip Aldworth, M.R.C.S., England, 1957, L.R.C.P., London, 1957, M.B., B.S., 1957 (Univ. *London), R.A.A.F., Canberra.*

Dalvell, Lindsay Elizabeth, M.B., B.S., 1956 (Univ. Sydney), 93 Cambrai Avenue, Engadine.

The undermentioned have been elected as members of the New South Wales Branch of the British Medical Association: Alexander, Michael, M.B., B.S., 1958 (Univ. Sydney); Cameron, Robert Stewart, M.B., B.S., 1958 (Univ. Sydney); Goldinberg, Jacob, M.D., 1923 (Univ. Warsaw) (registered under Section 17 (2A)); Hussain, Mohammed Yusuff, M.B., B.S., 1958 (Univ. Sydney); Kariks, Jekabs, M.D., 1949 (Univ. Tubingen), D.T.M. & H., Sydney, 1957 (registered under Section 17 (2B)); Mackenzie, Kenneth James, M.B., B.S., 1957 (Univ. Sydney); McLeod, James Graham, M.B., B.S., 1959 (Univ. Sydney); Robinson, Eleanor Mary, M.B., B.S., 1958 (Univ. Sydney); Runcie, Donald George, M.B., B.S., 1958 (Univ. Sydney); Snape, Geoffrey, M.B., B.S., 1957 (Univ. Sydney); Wong, Seow Choon, M.B., B.S., 1959 (Univ. Sydney).

Deaths.

THE following death has been notified:

GREENSHIELDS.—Hilda Adella Greenshields, on July 2, 1959, at Heidelberg, Victoria.

Diary for the Month.

SEPTEMBER 8.—New South Wales Branch, B.M.A.: Executive and Finance Committee.
SEPTEMBER 9.—Queensland Branch, B.M.A.; Council Meeting.
SEPTEMBER 10.—Queensland Branch, B.M.A.: Bancroft Oration.
SEPTEMBER 10.—New South Wales Branch, B.M.A.: Public Relations Committee.
SEPTEMBER 11.—Queensland Branch, B.M.A.: Fork Dinner.
SEPTEMBER 11.—Tasmanian Branch, B.M.A.: Branch Council.
SEPTEMBER 12.—Queensland Branch, B.M.A.: 4th Branch Convocation; Annual General Meeting.
SEPTEMBER 14.—Victorian Branch, B.M.A.: Finance Subcommittee.
SEPTEMBER 15.—New South Wales Branch, B.M.A.: Medical Politics Committee.

Medical Appointments: Important Notice.

MEDICAL PRACTITIONERS are requested not to apply for any appointment mentioned below without having first communicated with the Honorary Secretary of the Branch concerned, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

New South Wales Branch (Medical Secretary, 135 Macquarie Street, Sydney): All contract practice appointments in New South Wales.

South Australian Branch (Honorary Secretary, 80 Brougham Place, North Adelaide): All contract practice appointments in South Australia.

Editorial Notices.

ALL articles submitted for publication in this Journal should be typed with double or treble spacing. Carbon copies should not be sent. Authors are requested to avoid the use of abbreviations, other than those normally used by the Journal, and not to underline either words or phrases.

References to articles and books should be carefully checked. *In a reference to an article in a journal the following* information should be given: surname of author, initials of author, year, full title of article, name of journal, volume, number of first page of article. *In a reference to a book the* following information should be given: surname of author, initials of author, year of publication, full title of book, publisher, place of publication, page number (where relevant). *The abbreviations used for the titles of journals are those* of the list known as "World Medical Periodicals" (published by the World Medical Association). If a reference is made *to an abstract of a paper, the name of the original journal,* together with that of the journal in which the abstract has appeared, should be given with full date in each instance.

Authors submitting illustrations are asked, *if possible, to* provide the originals (not photographic copies) of line drawings, graphs and diagrams, and prints from the original negatives of photomicrographs. Authors who are not *accustomed to preparing drawings or photographic prints for* reproduction are invited to seek the advice of the Editor.

Original articles forwarded for publication are understood to *be offered to THE MEDICAL JOURNAL OF AUSTRALIA alone, unless* the contrary is stated.

All communications should be addressed to the Editor, THE *MEDICAL JOURNAL OF AUSTRALIA, The Printing House, Seamer* Street, Glebe, New South Wales. (Telephones: MW 2651-2-3.)

Members and subscribers are requested to notify the Manager, *THE MEDICAL JOURNAL OF AUSTRALIA, Seamer Street, Glebe,* New South Wales, without delay, of any irregularity in the delivery of this Journal. The management cannot accept any responsibility or recognize any claim arising out of non-receipt of journals unless such notification is received within one month.

SUBSCRIPTION RATES.—Medical students and others not receiving THE MEDICAL JOURNAL OF AUSTRALIA in virtue of *membership of the Branches of the British Medical Association* in Australia can become subscribers to the Journal by applying to the Manager or through the usual agents and booksellers. Subscriptions can commence at the *beginning of any quarter* and are renewable on December 31. The rate is £6 *per annum* within Australia and the British Commonwealth of Nations, and £7 10s. *per annum* within America and foreign countries, payable in advance.